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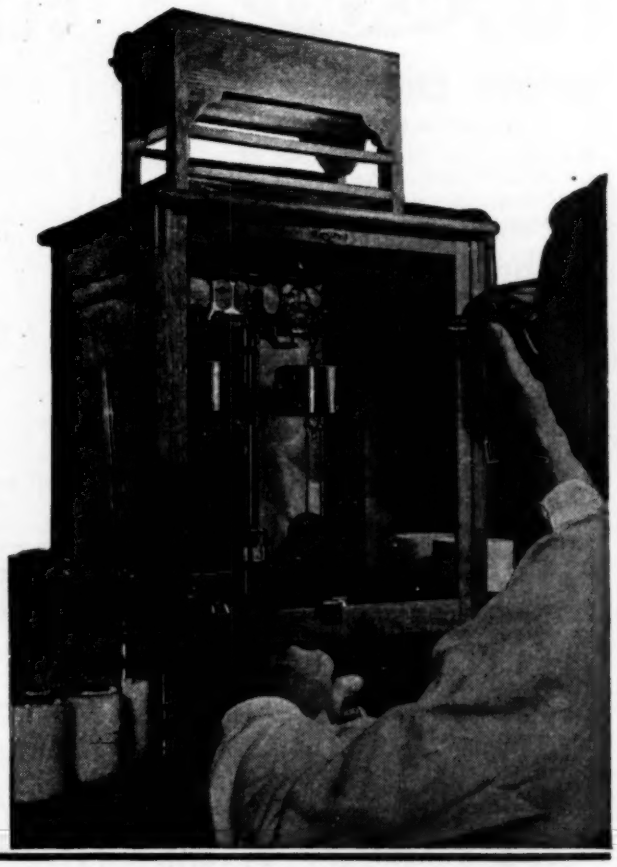

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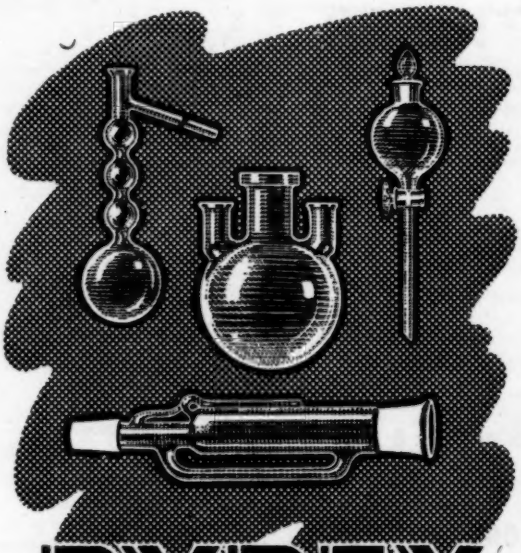

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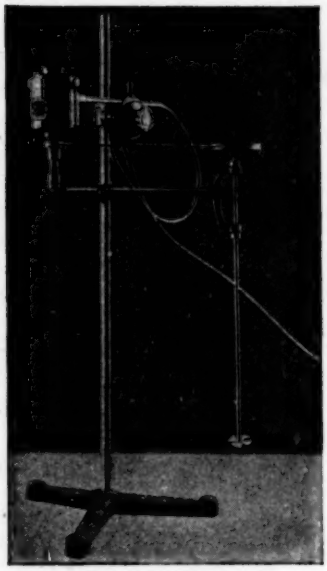

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ERRATA.

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Page.	Line.	
745	16	*for* " 2-nitro-1-naphthylamine " *read* " 1-nitro-2-naphthylamine."

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373	14 *	for " *Chem. and Ind.*" read " *J. Soc. Chem. Ind.*"
386	23 *	*for* " *ca.* 70% " *read* " *ca.* 90%."
394	Fig.	*for* " 50 " *in the scale of abscissæ, read* " 80."
397	29	*for* " $NR{:}N{\cdot}CO{\cdot}NH_2$ " *read* " $\overset{-}{O}\overset{+}{N}R{:}N{\cdot}CO{\cdot}NH_2$."
651	Fig. 2	transfer the title to Fig. 1 on p. 650.

* From bottom.

Sugden was an individualist. From his early youth he had been accustomed to fend for himself and to take full responsibility for his own affairs. He expected little from mankind, and was thus spared many possible disappointments. He deliberately limited the circle of his friends and the range of his interests, lest they should become a burden to him. From most organised groups of people he stood apart, and was the despair of those who sought his support for societies and clubs; but among a small group of his chosen friends he was happy, and his shrewd, dry humour would then find expression in conversation that often rose to brilliance. But for the most part he was a lonely man, and one who had learned to bear, if not to enjoy, a solitary life. His reference to a holiday in Touraine as having been spent " sitting under a banana tree reflecting on death, decay, and strong electrolytes," and his claim never to have been to a cinema, were largely figures of speech but nevertheless indicative of a real distaste for being caught up in a crowd.

He spoke French and German with some fluency and derived much quiet amusement from the exercise of his wit in these languages—to the delight of the wise and the discomfiture of the foolish. His individuality was much in evidence in the choice of his minor interests : he could speak with some authority on the seasonal variation in the exchange value of the French franc, on British silver coins issued since the reign of George I (of which he had a fine collection), and on the wines of Burgundy. To these diverse matters, as to his scientific work, he brought a characteristic acuteness of mind and a highly original outlook. In human affairs he showed an almost intuitive understanding of other people's views and feelings that enabled him to predict, often with uncanny accuracy, their actions under given conditions.

From the vast tapestry of life he selected for study a few particular areas. His artistry led him to choose neither the more highly coloured nor the more representational patches, but rather those that seemed somewhat dull and undistinguished. His genius enabled him to show that there was something unexpectedly interesting or bizarre in their structure or arrangement—a queer twist in the threads, an unsuspected knot, a peculiar relation of coloured strands—that threw a new light on the make-up of the whole gaudy pattern.

To him humans were nothing if not individuals. To those of us who held him in esteem and affection he was a very real and unusual person whom we remember as " J. N."

H. J. T. Ellingham.

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20. *Studies in the Polyene Series. Part XVII. Replacement Halogenation and Simultaneous Anionotropic Rearrangements of Acetylenylcarbinols and Glycols derived from αβ-Unsaturated Aldehydes.**

By I. M. Heilbron, E. R. H. Jones, R. N. Lacey, J. T. McCombie, and R. Raphael.

When the acetylenyl- or vinylacetylenyl-carbinols or acetylenyl glycols derived from αβ-unsaturated aldehydes are shaken with concentrated hydrochloric acid, at room temperature, replacement halogenation of the hydroxyl group accompanies the usual anionotropic rearrangement (see Parts VIII onwards). In the case of vinylethynylcarbinol (IV), which is unaffected by 25% sulphuric acid even at 100°, the rearranged chloro-compound (V) is readily obtained and is converted *via* the acetate into the primary acetylenylvinylcarbinol (VI), giving *n*-amyl alcohol on hydrogenation. The related glycol (XIV) from acraldehyde behaves analogously, leading eventually to octane-1 : 8-diol.

The expected light-absorption properties were observed with all the halogeno-compounds containing the conjugated vinylacetylene and *s*.-divinylacetylene chromophores.

The rearrangements of acetylenylcarbinols and glycols derived from αβ-unsaturated carbonyl compounds so far described in this series (Part VIII onwards, J., 1943—1944) consist almost entirely of examples involving a migrating hydroxyl anion. It has been postulated that the mobility of anionotropic systems increases with increasing stability of the mobile anion X, and hence with increasing strength of the acid HX (Burton and Ingold, J., 1928, 904; Burton, J., 1928, 1650). Consequently, it was to be expected that replacement-halogenation of propenylethynylcarbinol (I) and related compounds with reagents such as thionyl chloride or phosphorus pentachloride would lead to products, *e.g.*, (II), which, if they existed at all, would readily undergo rearrangement to chloro-alkylvinylacetylenes, *e.g.*, (III).

(I.) $CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH$
(II.) $CH_3{\cdot}CH{:}CH{\cdot}CHCl{\cdot}C{\vdots}CH$
(III.) $CH_3{\cdot}CHCl{\cdot}CH{:}CH{\cdot}C{\vdots}CH$

$CH_2{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH$ (IV.)
$CH_2Cl{\cdot}CH{:}CH{\cdot}C{\vdots}CH$ (V.)
$OH{\cdot}CH_2{\cdot}CH{:}CH{\cdot}C{\vdots}CH$ (VI.)

Reactions of this type with vinylethynylcarbinol (IV) were of particular interest, since this had been found to be unaffected by 25% sulphuric acid (Jones and McCombie, J., 1943, 261), and since its isomerisation product (VI) was required for syntheses of primary alcohols related to vitamin-A. When (IV) was caused to react in cold dilute ethereal solution with thionyl chloride in the presence of pyridine, a product was obtained which decomposed on attempted distillation, but under more vigorous conditions a mixture containing a high proportion of the chloro-hydrocarbon (V) resulted, as indicated by the ultra-violet absorption of the product (see below).

Since Campbell, Campbell, and Eby (*J. Amer. Chem. Soc.*, 1938, **60**, 2882) reported that treatment of methylethylethynylcarbinol with concentrated hydrochloric acid gave a 40% yield of 3-chloro-3-methylpent-

* See I.C.I. Ltd., Jones, and McCombie, B.P. 560,081.

1-yne, vinylethynylcarbinol (IV) was shaken with this acid for 40 minutes at 20—40°, whereby 1-*chloropent*-2-*en*-4-*yne* (V) was obtained in 50% yield. An indication of the structure of the chloro-compound was provided by its absorption spectrum (Table I) characteristic of the conjugated vinylacetylene system (see Parts VIII, X, XIV—XVI), and complete proof was furnished by its conversion into *n*-amyl alcohol by the following reactions.

TABLE I.

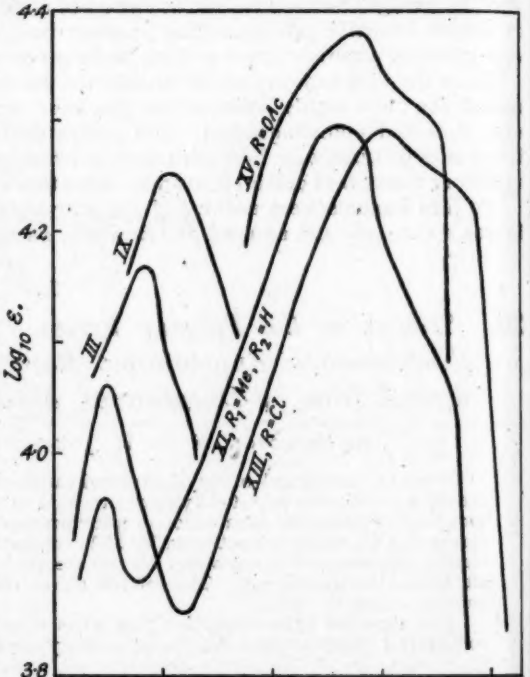
	$\lambda_{max.}$, A.	$\varepsilon_{max.}$		$\lambda_{max.}$, A.	$\varepsilon_{max.}$
1-Chloropent-2-en-4-yne (V)	2280	10,500	Pent-2-en-4-yn-1-ol (VI)	2230	14,000
2-Chlorohex-3-en-5-yne (III)	2260	14,000	,, acetate	2225	21,500
2-Chlorodec-3-en-5-yne (IX)*	2350	17,500	Hex-3-en-5-yn-2-ol [1]	2230	13,500
	2400*	17,000		2300*	9,500

* Inflexion.
[1] Jones and McCombie, J., 1943, 261.

Treatment of (V) with potassium acetate in methyl-alcoholic solution gave the *acetate* of pent-2-en-4-yn-1-ol (VI), together with a low-boiling fraction, probably the corresponding methyl ether. Both the acetate and the primary *alcohol* (VI) (*α-naphthylurethane*), obtained from it by alkaline hydrolysis, exhibit light absorption (Table I) similar to that of the parent chloro-hydrocarbon, indicating that all three substances contain the same conjugated system and that they must be interrelated in the manner prescribed. A Zerewitinoff determination on (VI) showed the presence of two active hydrogen atoms and on complete hydrogenation it gave *n*-amyl alcohol.

In order to ascertain at this stage whether (VI) reacts normally with carbonyl compounds, a Grignard reaction with butaldehyde was attempted according to the method evolved in Part XV. This gave a 30% yield of *non*-2-*en*-4-*yne*-1 : 6-*diol* (VII) (*bisphenylurethane*) with properties in accord with the suggested structure.

When propenylethynylcarbinol (I) was treated either with concentrated hydrochloric acid or with thionyl chloride and pyridine in the cold, good yields of 2-*chlorohex*-3-*en*-5-*yne* (III) (for absorption spectrum, see Table I and Fig.) were obtained. On the other hand, the action of hydrochloric acid on hex-3-en-5-yn-2-ol, the rearrangement product of (I), gave only a 45% yield of (III), accompanied by much material formed by addition of hydrogen chloride to the unsaturated system. With potassium acetate in methyl-alcoholic solution (III) gave the acetate of hex-3-en-5-yn-2-ol, identical in physical properties with that obtained by direct acetylation of the carbinol. A study has been made of various replacement reactions of (III), particularly those with amines, and this work will be described in due course.



The substituted propenylethynylcarbinol (VIII) is converted smoothly (85% yield) with concentrated hydrochloric acid into 2-*chlorodec*-3-*en*-5-*yne* (IX) (see Table I and Fig. for light absorption). Carbinols (X) prepared by condensing crotonaldehyde with vinylacetylenes also undergo rearrangement-chlorination and

$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH(OH) \cdot C{:}C \cdot CH{:}CH \cdot CH_2 \cdot OH$ (VII.)
$CH_3 \cdot [CH_2]_3 \cdot C{:}C \cdot CH(OH) \cdot CH{:}CH \cdot CH_3$ (VIII.)
$CH_3 \cdot [CH_2]_3 \cdot C{:}C \cdot CH{:}CH \cdot CHCl \cdot CH_3$ (IX.)

2-*chloro-octa*-3 : 7-*dien*-5-*yne* (XI; $R_1 = R_2 = H$), 2-*chloro*-7-*methylocta*-3 : 7-*dien*-5-*yne* (XI; $R_1 = Me$, $R_2 = H$), and 2-*chloro*-7-*methylnona*-3 : 7-*dien*-5-*yne* (XI; $R_1 = R_2 = Me$) have been prepared in this way. The structures of the rearranged chloro-compounds (IX and XI) are assumed by analogy with the simpler

(X.) $CHR_2{:}CR_1 \cdot C{:}C \cdot CH(OH) \cdot CH{:}CH \cdot CH_3$ $CHR_2{:}CR_1 \cdot C{:}C \cdot CH{:}CH \cdot CHCl \cdot CH_3$ (XI.)

cases where rigid proof has been provided, and the correctness of these assumptions is substantiated by light-absorption evidence (Table II and Fig.). The chloro-hydrocarbons of structure (XI) exhibit maximal absorption at about 2620 A. with inflexions at slightly longer wave-lengths, analogous to that already described for compounds containing the symmetrical dienyne chromophore (Parts X, XI, and XIV). The additional maxima at about 2200 A. of comparatively low intensity observed with these compounds appear to be characteristic.

In Part XI (Heilbron, Jones, and Raphael, J., 1943, 268) a dual rearrangement of the acetylenyl glycol (XII) from crotonaldehyde leading to a *s*.-divinylacetylenyl glycol (XIII; R = OH) was described. It has

TABLE II.

	$\lambda_{max.}$, A.	$\varepsilon_{max.}$
2-Chloro-octa-3 : 7-dien-5-yne (XI; $R_1 = R_2 = H$)	2200	6,000
	2620	17,000
	2750*	13,500
2-Chloro-7-methylnona-3 : 7-dien-5-yne (XI; $R_1 = R_2 = Me$)	2680	18,000
	2780*	15,500
2-Chloro-7-methylocta-3 : 7-dien-5-yne (XI; $R_1 = Me$, $R_2 = H$)	2190	7,500
	2625	18,000
	2750*	14,000
7-Methylnona-3 : 7-dien-5-yn-2-ol [1]	2640	16,500
	2690*	15,500

* Inflexion.

[1] Heilbron, Johnson, Jones, and Raphael, J., 1943, 265.

now been established that a similar change takes place on replacement halogenation of (XII) by treatment with concentrated hydrochloric acid, giving 2 : 9-*dichlorodeca*-3 : 7-*dien*-5-*yne* (XIII; R = Cl) in 85% yield, the light absorption-properties (Table III and Fig.) of which are similar, both in location and in intensity of the

(XII.) $CH_2{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{:}C{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}CH_3$ $CH_3{\cdot}CHR{\cdot}CH{:}CH{\cdot}C{:}C{\cdot}CH{:}CH{\cdot}CHR{\cdot}CH_3$ (XIII.)

main maximum, to those described (Part XI) for the corresponding glycol (XIII; R = OH), and the diacetate of the latter was obtained by treating the dichloro-compound with potassium acetate in alcohol.

TABLE III.

	$\lambda_{max.}$, A.	$\varepsilon_{max.}$
1 : 8-Dichloro-octa-2 : 6-dien-4-yne (XV; R = Cl)	2690	17,500
	2780*	15,500
2 : 9-Dichlorodeca-3 : 7-dien-5-yne (XIII; R = Cl)	2210	11,500
	2700	19,500
	2760	18,500
Deca-3 : 7-dien-5-yne-2 : 9-diol [1] (XIII; R = OH)	2180	11,000
	2650	21,500
	2800	19,000
1 : 8-Diacetoxyocta-2 : 6-dien-4-yne (XV; R = OAc)	2650	24,000
	2770*	21,000
Octa-2 : 6-dien-4-yne-1 : 8-diol (XV; R = OH) (crude)	2190	7,500
	2290	6,500
	2650	16,000
	2790	12,500
Diacetate [1] of deca-3 : 7-dien-5-yne-2 : 9-diol [1] (XIII; R = OAc)	2560	14,000
	2650	22,000
	2780	18,500

* Inflexions.

[1] Heilbron, Jones, and Raphael, J., 1943, 268.

The glycol (XIV) (Dupont, *Ann. Chim.*, 1913, **30**, 485) derived from acraldehyde failed to undergo rearrangement on treatment with 25% sulphuric acid, thus behaving analogously to the related ethynylcarbinol (Jones and McCombie, *loc. cit.*) and phenylvinylcarbinol (Burton and Ingold, *loc. cit.*). With concentrated hydrochloric acid, however, rearrangement-chlorination occurred, although the 1 : 8-*dichloro-octa*-2 : 6-*dien*-4-*yne* (XV; R = Cl) could not effectively be separated from the small quantity of unchanged glycol present in the product. It seems possible that in this case the reaction proceeds to an equilibrium point. However, when the dichloro-compound was treated with potassium acetate in methyl alcohol, 1 : 8-*diacetoxyocta*-2 : 6-*dien*-4-*yne* (XV;

(XIV.) $CH_2{:}CH{\cdot}CH(OH){\cdot}C{:}C{\cdot}CH(OH){\cdot}CH{:}CH_2$ $CH_3R{\cdot}CH{:}CH{\cdot}C{:}C{\cdot}CH{:}CH{\cdot}CH_2R$ (XV.)

R = OAc) was readily isolated in a pure condition, and on complete hydrogenation, followed by hydrolysis of the di-ester, octane-1 : 8-diol (bisphenylurethane) was obtained. Direct hydrolysis of the diacetate gave a diol (*bisphenylurethane*) which underwent extensive polymerisation on distillation even in a high vacuum, presumably owing to formation of a polymeric ether.

Attempts were made to obtain the dichloro-diene (XVI), which can be regarded as a substituted chloroprene, by more vigorous treatment of hex-3-en-5-yn-2-ol or 2-chlorohex-3-en-5-yne (III) with hydrochloric acid. From either the former with concentrated acid at 55°, or from (III) under conditions similar to those used by Carothers, Berchet, and Collins (*J. Amer. Chem. Soc.*, 1932, **54**, 4066) for the conversion of vinylacetylene

$CH_2{\cdot}CHCl{\cdot}CH{:}CH{\cdot}CCl{:}CH_2$ (XVI.)

into 2-chlorobutadiene, complex mixtures were obtained. By careful fractionation, however, a dichloro-diene, provisionally designated by analogy as 2 : 5-*dichlorohexa*-1 : 3-*diene* (XVI), and showing the expected high-intensity light absorption, was isolated.

Several attempts have been made to prepare bromo-compounds corresponding to the various chloro-compounds described above, but when (I), (IV), and (XII) were treated with hydrobromic acid, highly unstable heterogeneous products, decomposing on attempted distillation, resulted. In this connection the work of Favorskaya *et al.* (*J. Gen. Chem. Russ.*, 1940, **10**, 461; 1939, **9**, 386) is of interest, since they observed that by treating dimethylethynylcarbinol (XVII) with hydrobromic acid, the bromo-compound rapidly isomerised through the allene (XVIII) to the 1 : 3-butadiene derivative (XIX). The primary chloro-compound, on the

$CMe_2(OH){\cdot}C{:}CH \longrightarrow CMe_2{:}C{:}CHBr \longrightarrow CH_2{:}CMe{\cdot}CH{:}CHBr$
(XVII.) (XVIII.) (XIX.)

other hand, prepared with hydrochloric acid in the presence of cuprous and ammonium chlorides, was much more stable, giving the allene only after a reaction time of some days and isomerising to the conjugated diene only after three weeks. The instability of the bromo-compounds obtained in the present study may well be occasioned by the ease with which rearrangements of the above type occur.

Experimental.

(Absorption spectra were determined in alcoholic solutions.)

1-*Chloropent*-2-*en*-4-*yne* (V).—A mixture of vinylethynylcarbinol (40 g.; Jones and McCombie, J., 1942, 733) and concentrated hydrochloric acid (200 c.c.) was shaken at 20° for 30 minutes under nitrogen and finally for 10 minutes at 40°. The product, isolated by means of ether, gave 1-*chloropent*-2-*en*-4-*yne* (30 g.), b. p. 82—84°/200 mm., $n_D^{18°}$ 1·4842 (Found ; Cl, 35·0. C_5H_5Cl requires Cl, 35·3%). Even at 0° in the presence of quinol, the chloro-compound darkened rapidly.

1-*Acetoxypent*-2-*en*-4-*yne*.—A solution of 1-chloropent-2-en-4-yne (24 g.) and anhydrous potassium acetate (60 g.) in methyl alcohol (300 c.c.) was heated under reflux for 18 hours under nitrogen. The potassium chloride was filtered off, the major portion of the solvent distilled off through a column, and the residue poured into water. Distillation of the product obtained by isolation with ether gave three fractions: (1) B. p. 82—86°/100 mm., $n_D^{22°}$ 1·4446; (2) b. p. 86—90°/100 mm., $n_D^{22°}$ 1·4567; (3) 1-*acetoxypent*-2-*en*-4-*yne* (8 g.), b. p. 72°/18 mm., $n_D^{19°}$ 1·4863 (Found: C, 67·4; H, 6·6. $C_7H_8O_2$ requires C, 67·75; H, 6·5%). *Active hydrogen* (Zerewitinoff): The acetate (145 mg.) gave (without heating) 29·2 c.c. of methane at 23°/767 mm. (1·0 active hydrogen atom per mol.).

Pent-2-*en*-4-*yn*-1-*ol* (VI).—The above acetate (8 g.) was shaken for 1 hour with aqueous potassium hydroxide (400 c.c.; 2·5%) under nitrogen. The reaction mixture was saturated with salt and repeatedly extracted with small portions of ether, and from the extracts there were obtained 4·5 g. of *pent*-2-*en*-4-*yn*-1-*ol*, b. p. 103°/100 mm., 90°/50 mm., $n_D^{23°}$ 1·4933 (Found: C, 73·05; H, 7·2. C_5H_6O requires C, 73·15; H, 7·35%). *Active hydrogen* (Zerewitinoff): The carbinol (56 mg.) gave 30·3 c.c. of methane at 20°/767 mm. (1·9 active hydrogen atoms per mol.). The *α-naphthylurethane* crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 110—111° (Found: N, 5·8. $C_{16}H_{13}O_2N$ requires N, 5·6%). The overall yield of (VI) from acraldehyde is only about 4%.

The carbinol (3·4 g.) in methyl acetate (20 c.c.) was shaken with hydrogen in the presence of platinic oxide (100 mg.) until absorption was complete. The catalyst and solvent were removed, the latter through a column, and the residual *n*-amyl alcohol had b. p. 136—138°, $n_D^{18°}$ 1·4103 (lit. b. p. 137·8°, $n_D^{15°}$ 1·4117). The α-naphthylurethane had m. p. 68°, undepressed on admixture with an authentic specimen (Bicket and French, *J. Amer. Chem. Soc.*, 1926, **48**, 747, give m. p. 68°).

Non-2-*en*-4-*yne*-1 : 6-*diol* (VII).—A solution of pent-2-en-4-yn-1-ol (4·5 g.) in ether (100 c.c.) was added slowly with stirring to ethylmagnesium bromide (from 2·7 g. of magnesium) in an atmosphere of nitrogen; the reaction was completed by heating under reflux for 2 hours. *n*-Butaldehyde (4 g.) in ether (100 c.c.) was then added in the cold, and the mixture subsequently refluxed for 1½ hours. The dark red reaction mixture was decomposed with ammonium chloride, and isolation of the product with ether gave the *glycol* (2·5 g.) as a colourless viscous oil, b. p. 85° (bath temp.)/10^{-4} mm., $n_D^{20°}$ 1·5112 (Found: C, 69·85; H, 9·3. $C_9H_{14}O_2$ requires C, 70·1; H, 9·2%). *Active hydrogen* (Zerewitinoff): The glycol (68 mg.) gave 19·1 c.c. of methane at 23°/758 mm. (1·8 active hydrogen atoms per mol.). *Quantitative hydrogenation*: A mixture of the glycol (500 mg.) and platinic oxide (100 mg.) in ethyl acetate (10 c.c.) absorbed 218 c.c. of hydrogen at 21°/765 mm. (= 2·8). *Light absorption*: Maximum, 2280 A.; ε = 16,000. Inflexion, 2380 A.; ε = 10,000. The *bisphenylurethane* crystallised from benzene–light petroleum (b. p. 60—80°) in needles, m. p. 84° (Found: N, 7·4. $C_{23}H_{24}O_4N_2$ requires N, 7·15%).

2-*Chlorohex*-3-*en*-5-*yne* (III).—(*a*) A mixture of propenylethynylcarbinol (70 g.; Jones and McCombie, *loc. cit.*) and concentrated hydrochloric acid (200 c.c.) was shaken at 20° under nitrogen for 20 minutes, and the oily layer separated by means of ether. After washing and drying, evaporation yielded 2-*chlorohex*-3-*en*-5-*yne* (62 g.), b. p. 72—75°/100 mm., $n_D^{19°}$ 1·4832, as a colourless oil which rapidly darkened on standing, although the pure colourless chloro-compound can be recovered almost quantitatively on redistillation (Found: Cl, 31·1. C_6H_7Cl requires Cl, 31·0%).

(*b*) To a solution of propenylethynylcarbinol (20 g.) and anhydrous pyridine (22 g.) in dry ether (150 c.c.) at 0°, redistilled thionyl chloride (29·5 g.) was added during an hour with stirring after which the mixture was set aside overnight at 0°. After treatment with ice the ethereal solution was worked up in the usual manner, yielding 2-chlorohex-3-en-5-yne (13·5 g.), b. p. 131°, 111°/400 mm., $n_D^{20°}$ 1·4824.

2-*Acetoxyhex*-3-*en*-5-*yne*.—2-Chlorohex-3-en-5-yne (20 g.) was added to a solution of anhydrous sodium acetate (25 g.) in alcohol (120 c.c.) which was then heated under reflux for 6 hours. After dilution with water, the product was isolated with ether and the ethereal solution dried and evaporated. On distillation the material boiled over a wide range, owing probably to the presence of the ethyl ether, but redistillation of the fraction, b. p. 85—97° (mainly 92—97°)/50 mm. (8·2 g.), gave 2-acetoxyhex-3-en-5-yne (5 g.), b. p. 94—96°/50 mm., $n_D^{18·5°}$ 1·4589 (Jones and McCombie, *loc. cit.*, give b. p. 101—103°/70 mm., $n_D^{18·5°}$ 1·4578). *Light absorption*: Maximum, 2240 A., ε = 12,500.

2-*Chlorodec*-3-*en*-5-*yne* (IX).—A mixture of dec-2-en-5-yn-4-ol (5 g.; Heilbron, Jones, and Raphael, J., 1943, 264) and concentrated hydrochloric acid (25 c.c.) was shaken at 20° for 30 minutes in an atmosphere of nitrogen. Isolation of the product with ether gave 2-*chlorodec*-3-*en*-5-*yne* (4·7 g.), b. p. 58°/1 mm., $n_D^{18°}$ 1·4947 (Found: Cl, 20·75. $C_{10}H_{15}Cl$ requires Cl, 20·85%).

2-*Chloro-octa*-3 : 7-*dien*-5-*yne* (XI; $R_1 = R_2 = H$).—Octa-2 : 7-dien-5-yn-4-ol (10 g.; Heilbron, Jones, and Weedon, J., 1944, 140) was shaken with concentrated hydrochloric acid (50 c.c.) and ether (5 c.c.) under nitrogen for 1 hour. After dilution with water the product was isolated by ether extraction, 2-*chloro-octa*-3 : 7-*dien*-5-*yne* (8 g.) being obtained as a colourless liquid, b. p. 48—50°/3 mm., $n_D^{16°}$ 1·5406 (Found: C, 68·15; H, 6·55. C_8H_9Cl requires C, 68·35; H, 6·45%).

2-*Chloro*-7-*methylocta*-3 : 7-*dien*-5-*yne* (XI; R_1 = Me, R_2 = H).—An experiment similar to that described above employing 7-methylocta-2 : 7-dien-5-yn-4-ol (8 g.; Heilbron, Jones, and Weedon, *loc. cit.*) yielded 2-*chloro*-7-*methylocta*-3 : 7-*dien*-5-*yne* (5 g.), b. p. 46°/3 mm., $n_D^{18°}$ 1·5302 (Found: C, 70·15; H, 7·1. $C_9H_{11}Cl$ requires C, 69·9; H, 7·2%).

2-*Chloro*-7-*methylnona*-3 : 7-*dien*-5-*yne* (XI; $R_1 = R_2$ = Me).—A mixture of 7-methylnona-2 : 7-dien-5-yn-4-ol (8 g.; Heilbron, Johnson, Jones, and Raphael, J., 1943, 265) and concentrated hydrochloric acid (40 c.c.) was shaken at 20° for 30 minutes under nitrogen. 2-*Chloro*-7-*methylnona*-3 : 7-*dien*-5-*yne* (7 g.), isolated in the usual manner, had b. p. 71—72°/1 mm., $n_D^{20°}$ 1·5262 (Found: Cl, 21·3. $C_{10}H_{15}Cl$ requires Cl, 21·05%).

2 : 9-*Dichlorodeca*-3 : 7-*dien*-5-*yne* (XIII; R = Cl).—A solution of deca-2 : 8-dien-5-yn-4 : 7-diol (2 g.; Heilbron, Jones, and Raphael, J., 1943, 268) in ether (10 c.c.) was shaken with concentrated hydrochloric acid (30 c.c.) for 45 minutes at 20° under nitrogen. The reaction mixture was diluted with water and extracted with ether. From the washed and dried ethereal phase 2 : 9-*dichlorodeca*-3 : 7-*dien*-5-*yne* (2·1 g.) was isolated as a mobile liquid which gradually darkened on keeping; b. p. 100—102°/10^{-2} mm., $n_D^{25°}$ 1·5500 (Found: C, 59·5; H, 6·2. $C_{10}H_{12}Cl_2$ requires C, 59·1; H, 5·9%). The dichloro-compound gives an immediate precipitate with cold aqueous silver nitrate.

2 : 9-*Diacetoxydeca*-3 : 7-*dien*-5-*yne* (XIII; R = OAc).—The above dichloro-compound (2 g.) was added to a solution of anhydrous potassium acetate (2·5 g.) in methyl alcohol (30 c.c.), which was then heated under reflux for 30 minutes. After dilution with water the product was extracted with ether, yielding the diacetate (1·8 g.), b. p. 138—139°/10^{-2} mm., $n_D^{22°}$ 1·4995 (when prepared from the rearranged glycol it had b. p. 131—132°/10^{-2} mm., $n_D^{27°}$ 1·5005).

Octa-1 : 7-*dien*-4-*yne*-3 : 6-*diol* (XIV) (cf. Dupont, *loc. cit.*).—To an ethereal solution of acetylenedimagnesium bromide (from magnesium, 12 g.), a solution of acraldehyde (28 g.) in ether (30 c.c.) was added during 30 minutes with vigorous

stirring, which was continued for a further 4 hours. The Grignard complex was decomposed with a saturated solution of ammonium chloride (200 c.c.), and the acraldehyde polymer (15 g.) filtered off. The ethereal solution furnished octa-1 : 7-dien-4-yne-3 : 6-diol (10 g.), a viscous liquid, b. p. 131°/5 mm., 112—114°/1 mm., $n_D^{20°}$ 1·5011 (Dupont, *loc. cit.* gives b. p. 146°/15 mm., n_D 1·5040). It shows no absorption of high intensity in the ultra-violet. The glycol was recovered unchanged on shaking for 24 hours with 25% sulphuric acid.

1 : 8-*Dichloro-octa*-2 : 6-*dien*-4-*yne* (XV; R = Cl).—A solution of the above glycol (5 g.) in ether (5 c.c.) was shaken with concentrated hydrochloric acid (25 c.c.) at 20° for 45 minutes under nitrogen. The reaction mixture was extensively diluted with water, and the product, obtained by extraction with ether and repeated distillation, was slightly impure 1 : 8-*dichloro-octa*-2 : 6-*dien*-4-*yne* (6 g.), b. p. 95—97°/10^{-3} mm., $n_D^{24°}$ 1·5700 (Found : C, 56·3, 56·3; H, 5·0, 5·4. $C_8H_8Cl_2$ requires C, 54·9; H, 4·6%). It has not been found possible to separate the pure dichloro-compound from the small quantity of glycol which it undoubtedly contains. The product gives an immediate precipitate with cold aqueous silver nitrate.

1 : 8-*Diacetoxyocta*-2 : 6-*dien*-4-*yne* (XV; R = OAc).—The above dichloro-compound (6 g.) was heated under reflux for 8 hours in nitrogen with a solution of anhydrous potassium acetate (10 g.) in methyl alcohol (100 c.c.). The reaction mixture was diluted with water and extracted with ether, and distillation of the washed and dried ethereal phase gave two fractions : (i) B. p. 82—84°/10^{-4} mm. (2 g.), $n_D^{20°}$ 1·5691, and (ii) 1 : 8-*diacetoxyocta*-2 : 6-*dien*-4-*yne* (3 g.), b. p. 118—120°/10^{-4} mm., $n_D^{20°}$ 1·5301 (Found : C, 64·5; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·85; H, 6·35%). When the diacetate (4 g.) was heated under reflux, in nitrogen, with methyl-alcoholic potassium hydroxide (50 c.c.; 6%) for 4 hours, the product, isolated with ether, underwent extensive decomposition on distillation, even at 10^{-4} mm. A small amount (200 mg.) of the glycol, not sufficiently pure to justify analysis, was obtained which had b. p. 110—112°/10^{-4} mm., $n_D^{16°}$ 1·5430. The *bisphenylurethane* of *octa*-2 : 6-*dien*-4-*yne*-1 : 8-*diol* could be obtained, however, and it formed prismatic plates or needles, m. p. 162°, from benzene (Found : N, 7·8. $C_{22}H_{18}O_4N_2$ requires N, 7·45%).

Octane-1 : 8-*diol*.—A solution of 1 : 8-diacetoxyocta-2 : 6-dien-4-yne (2 g.) in methyl alcohol (10 c.c.) was hydrogenated in the presence of platinic oxide (10 mg.). When absorption ceased the solution was freed from catalyst by filtration, a solution of potassium hydroxide (2 g.) in methyl alcohol (30 c.c.) was added, and the mixture heated under reflux for 3 hours. Isolation by means of ether and subsequent distillation gave octane-1 : 8-diol, b. p. 170—171°/16 mm., which solidified in contact with light petroleum (b. p. 40—60°), and on crystallisation from a mixture of this solvent with benzene it separated as needles, m. p. 62° (Lespieau, *Ann. Chim.*, 1914, **2**, 287, gives b. p. 172°/20 mm., m. p. 62—63°). The bisphenylurethane crystallised from ethyl acetate as plates, m. p. 173° (Lespieau, *loc. cit.*, gives m. p. 172—172·5°).

Reaction of Hex-3-en-5-yn-2-ol with Concentrated Hydrochloric Acid.—(*a*) A mixture of the carbinol (30 g.; Jones and McCombie, J., 1943, 261) and concentrated hydrochloric acid (100 c.c.) was shaken at 20° for 20 minutes. Distillation of the product obtained by isolation with ether gave two fractions : (i) Mainly 2-chlorohex-3-en-5-yne, b. p. 85—87°/150 mm. (15 g.), $n_D^{20°}$ 1·4801; (ii) b. p. 91°/50 mm., 76°/18 mm. (8 g.), $n_D^{20°}$ 1·5097.

(*b*) The carbinol (95 g.) was added during 10 minutes to vigorously stirred concentrated hydrochloric acid at 55° under nitrogen, stirring and heating being continued for 30 minutes. The mixture was then diluted with water, the product isolated by means of ether, and distilled through a Widmer column. Two main fractions were collected : (i) Mainly 2-chlorohex-3-en-5-yne, b. p. 70—97°/100 mm. (33 g.), $n_D^{19°}$ 1·4826; (ii) b. p. 68—78°/15 mm. (66·5 g.), $n_D^{18°}$ 1·5190. Further fractionation of (ii) through the packed column described below gave a product (27 g.) consisting essentially of dichloro-diene, probably 2 : 5-*dichlorohexa*-1 : 3-*diene*, b. p. 79—81°/17 mm., $n_D^{19°}$ 1·5225 (Found : Cl, 47·2. $C_6H_8Cl_2$ requires Cl, 47·0%). *Light absorption :* Maximum, 2445 A.; $E^{1\%}_{1\text{ cm.}}$ 1420.

Addition of Hydrogen Chloride to 2-*Chlorohex*-3-*en*-5-*yne*.—The chloro-compound (150 g.) was shaken at about 20° for 4 hours with a solution of cuprous chloride (75 g.) and ammonium chloride (30 g.) in concentrated hydrochloric acid (500 c.c.), the product being isolated with ether after steam-distillation. The residual oil was fractionated through a well-lagged column containing a 40 × 1·8 cm. packing of single-turn glass helices and fitted with a total condensation–variable take-off head adjusted to give a reflux ratio of about 8 : 1. After much starting material had been stripped off, the following fractions were obtained : (i) B. p. 55—68°/15 mm. (10 g.), $n_D^{21°}$ 1·4988; (ii) b. p. 68—75°/15 mm. (14 g.), $n_D^{21°}$ 1·5092; (iii) b. p. 75—76°/15 mm. (19 g.), $n_D^{21°}$ 1·5179; (iv) b. p. 76—78°/15 mm. (10 g.), $n_D^{21°}$ 1·5251; (v) b. p. 78—79°/15 mm. (14·5 g.), $n_D^{21°}$ 1·5273. Attempts further to fractionate (iii), (iv), and (v) resulted in no appreciable variation in physical constants.

Light absorption : Fraction (iii). Maximum, 2380 A.; $E^{1\%}_{1\text{ cm.}}$ 1300 (Found : Cl, 44·6. Calc. for $C_6H_8Cl_2$: Cl, 47·0%). Fraction (iv). Maximum, 2410 A.; $E^{1\%}_{1\text{ cm.}}$ 1450 (Found : Cl, 46·7%). Fractions (iv) and (v) are considered to consist essentially of 2 : 5-dichlorohexa-1 : 3-diene.

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21. *Studies in the Polyene Series. Part XVIII. The Formation of Ethers from Propenylethynylcarbinol and Related Compounds.*

By I. M. HEILBRON, E. R. H. JONES, and B. C. L. WEEDON.

Isomerisation of propenylethynylcarbinol (I) with sulphuric acid in alcoholic solution gives the ethers (II; R = OMe and OEt) of the conjugated vinylethynylcarbinols. The etherification appears to occur essentially as a consequence of the anionotropic rearrangement. An analogous dual etherification-isomerisation can be effected with the acetylenyl glycol (III) from crotonaldehyde.

When the carbinol (I) is distilled in the presence of a small quantity of sulphuric acid, self-etherification accompanies the rearrangement, yielding the divinylacetylenyl C_{12} ether (V).

An improved procedure for the preparation of propenylethynylcarbinol (I) is described.

SEVERAL methods of obtaining ethers of acetylenylcarbinols are known but the most effective appears to consist simply in treating the carbinol with the appropriate alcohol in the presence of concentrated sulphuric acid (Moureu, Dufraisse, and Blatt, *Bull. Soc. chim.*, **1924**, **35**, 1412; Dufraisse and Rocher, *ibid.*, 1935, **2**, 2235). This method appears to be applicable particularly to tertiary carbinols, and Nazarov (*Bull. Acad. Sci. U.R.S.S.*,

1938, 706), who used alcoholic sulphuric acid at 50—80° to make ethers of vinylacetylenylcarbinols of the type $CH_2{:}CH{\cdot}C{:}C{\cdot}C(OH)R_1R_2$, mentions that secondary alcohols form ethers only with difficulty.

A convenient synthesis of ethers of ethynyl- and vinylacetylenyl-carbinols derived from αβ-unsaturated carbonyl compounds was desired, and it seemed possible that compounds such as (II) might be obtained by effecting the anionotropic rearrangement (Jones and McCombie, J., 1943, 261) of propenylethynylcarbinol (I) in the presence of an excess of the required alcohol, using concentrated sulphuric acid. This proved to be the case, and when the carbinol (I) was treated with methyl-alcoholic sulphuric acid at 20°, 2-*methoxyhex*-3-*en*-

(I.) $CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{:}CH$ $CH_3{\cdot}CHR{\cdot}CH{:}CH{\cdot}C{:}CH$ (II.)

5-*yne* (II; R = OMe) was isolated in 65% yield. The *ethyl ether* (II; R = OEt) was obtained (40% yield) in an analogous manner. The high volatility of these ethers renders their isolation difficult, and better yields could undoubtedly be obtained by a more detailed study of the reaction conditions. The structures of the two ethers are adequately established by their absorption spectra (Table) which are characteristic of the conjugated vinylacetylene chromophore (see Parts VIII—X, XIV—XVII). Further evidence is forthcoming from the observation that the methyl ether can also be isolated from the product obtained by treating 2-chlorohex-3-

	$\lambda_{max.}$, A.	$\varepsilon_{max.}$
2-Methoxyhex-3-en-5-yne (II; R = OMe)	2235	12,500
	*2320	11,000
2-Ethoxyhex-3-en-5-yne (II; R = OEt)	2230	12,500
	*2290	10,500
Hex-3-en-5-yn-2-ol [1] (II; R = OH)	2230	13,500
	*2300	9,500
Di-2-(hex-3-en-5-ynyl) ether (V)	2240	26,500
	*2310	23,000
2 : 9-Diethoxydeca-3 : 7-dien-5-yne (IV; R = OEt)	2650	23,000
	2800	17,000
Deca-3 : 7-dien-5-yne-2 : 9-diol [2] (IV; R = OH)	2650	21,500
	2800	19,000

* Inflexion.

[1] Jones and McCombie, *loc. cit.* [2] Heilbron, Jones, and Raphael, J., 1943, 268.

en-5-yne (II; R = Cl), described in the preceding paper, with methyl alcohol in the presence of pyridine or other bases.

No ether formation could be detected when the rearrangement product of (I), *i.e.*, hex-3-en-5-yn-2-ol (II; R = OH), was treated with methyl alcohol and sulphuric acid. This supports Nazarov's finding (*loc. cit.*) that secondary carbinols cannot readily be etherified in this way and, together with the results described in the next paragraph, provides a strong indication that etherification occurs during, and as a result of, the anionotropic rearrangement under the influence of acids.

It was observed by Moureu, Dufraisse, and Houghton (*Bull. Soc. chim.*, 1927, **41**, 53) that the tertiary acetate, $CPh_2(OAc){\cdot}C{:}C{\cdot}Ph$, could be converted into the corresponding methyl ether merely by heating it with methyl alcohol. No such conversion could be effected with the acetate of (I) by boiling with methyl alcohol for 6 hours, and a repetition of the experiment in the presence of anhydrous potassium carbonate merely resulted in hydrolysis. The failure of the first experiment appears to be due only partly to the fact that (I) is a secondary carbinol, and more especially to the comparatively low mobility of the propenylethynyl system, since etherification does occur in the case of the acetate of a more readily isomerised secondary carbinol (see Part XX).

It is noteworthy that although conjugated vinylacetylenes, particularly *s*.-divinylacetylenes, undergo Diels–Alder addition reactions (Norton, *Chem. Reviews*, 1942, **31**, 319), yet no reaction could be induced between the ether (II; R = OMe) and maleic anhydride in benzene solution, even at 150°.

The dual rearrangement of the acetylenyl glycol (III), derived from crotonaldehyde, to the *s*.-divinylacetylenyl glycol (IV; R = OH) has already been described (Part XI). In the presence of alcoholic sulphuric acid, simultaneous etherification accompanies the isomerisation, yielding 2 : 9-*diethoxydeca*-3 : 7-*dien*-5-*yne* (IV; R = OEt), which exhibits light absorption similar to that of the corresponding glycol.

(III.) $CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{:}C{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}CH_3$ $CH_3{\cdot}CHR{\cdot}CH{:}CH{\cdot}C{:}C{\cdot}CH{:}CH{\cdot}CHR{\cdot}CH_3$ (IV.)

One experiment involving the rearrangement of propenylethynylcarbinol (I) in the usual manner with dilute sulphuric acid proceeded anomalously, the main product being a liquid of much higher b. p. than the expected isomeride (II; R = OH). Attempts to repeat this experiment were fruitless until, investigating the possibility that all traces of acid had not been removed prior to distillation of the product, we distilled the carbinol (I) with a small quantity of dilute sulphuric acid, whereupon this high-boiling compound, which proved to be a C_{12} ether, was produced in 45% yield. This ether must be *di*-2-(*hex*-3-*en*-5-*ynyl*) *ether*, $O(CHMe{\cdot}CH{:}CH{\cdot}C{:}CH)_2$ (V), since (*a*) it exhibits intense light absorption (Table) corresponding to the presence of two conjugated vinylacetylene systems in the molecule, (*b*) it readily forms a silver salt with ammoniacal silver nitrate, and (*c*) on complete hydrogenation it gives a compound which is probably di-2-(*n*-hexyl) ether. This self-etherification reaction is quite analogous to the simple etherification described above, and in

accordance with this view, treatment of the rearranged carbinol (II; R = OH) with sulphuric acid in a similar fashion gave a much poorer yield of (V).

The n-*butyl ether* of propenylethynylcarbinol (I) was obtained, although in very low yield, by treatment of the intermediate sodio-compound, obtained by condensing crotonaldehyde with sodium acetylide, with an excess of the appropriate alkyl bromide. The replacement reaction would appear to be largely incomplete in liquid ammonia solution since much of the carbinol (I) was also isolated, but no trace of the *C*-alkylated product was obtained.

In Part VI (J., 1942, 733) the preparation of propenylethynylcarbinol (I) from crotonaldehyde and sodium acetylide in liquid ammonia solution was described, the sodium acetylide employed in this and related preparations being prepared *in situ* directly from sodium. It has now been found preferable to obtain the sodium acetylide from sodamide, the latter being prepared by means of a ferric nitrate–sodium oxide catalyst (Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120); the acetylide appears to be produced in a considerably more reactive condition than that formed by the direct interaction of acetylene with sodium in liquid ammonia. By using this method the preparation of propenylethynylcarbinol has now been appreciably improved in that, not only can yields of 75% be obtained regularly, but the main operations involved in an experiment on a 15 M. scale can be completed in about 14 hours. Similarly improved results have been obtained in other preparations of ethynylcarbinols. Hennion and Lieb (*J. Amer. Chem. Soc.*, 1944, **66**, 1289) describe a preparation of propenylethynylcarbinol which gives a 46% yield.

Experimental.

(Absorption spectra were determined in alcoholic solutions.)

2-Methoxyhex-3-en-5-yne (II; R = OMe).—(*a*) Propenylethynylcarbinol (250 g.; see below) was added to a solution of concentrated sulphuric acid (125 g.) in dry methyl alcohol (1·25 l.), and the mixture kept at 20° for a week. After dilution (to 5 l.) with water, the product was isolated by means of ether, and distillation through a 24-cm. Dufton column gave *2-methoxyhex-3-en-5-yne* (190 g.), b. p. 73—76·5° (mainly 75—76°)/120 mm., $n_D^{17°}$ 1·4537. The ether is a colourless mobile liquid with a pleasant odour (Found: C, 76·65; H, 9·4. $C_7H_{10}O$ requires C, 76·35; H, 9·15%). *Active hydrogen* (Zerewitinoff): The ether (71·5 mg.) gave 15·15 c.c. of methane (after heating to 90°) at 15°/765 mm., equivalent to 1·0 active hydrogen atom per mol.

When hex-3-en-5-yn-2-ol (18 g.; Jones and McCombie, J., 1943, 261) was added to a solution of concentrated sulphuric acid (9 g.) in methyl alcohol (90 c.c.) and the mixture kept for a week, no trace of the methyl ether was obtained on working up by the above method.

(*b*) A mixture of 2-chlorohex-3-en-5-yne (50 g.; previous paper), pyridine (50 g.), and dry methyl alcohol (50 g.) was refluxed for 17 hours. After dilution with dilute hydrochloric acid, isolation with ether gave 2-methoxyhex-3-en-5-yne (9 g.), b. p. 73—77°/120 mm., $n_D^{14·5°}$ 1·4547.

2-Ethoxyhex-3-en-5-yne (II; R = OEt).—Prepared by the method described under (*a*) above from the carbinol (30 g.), concentrated sulphuric acid (12 g.), and dry alcohol (120 c.c.), the *ether* (16 g.), a pleasant-smelling mobile liquid, had b. p. 81—81·5°/100 mm., $n_D^{14°}$ 1·4532 (Found: C, 77·6; H, 9·6. $C_8H_{12}O$ requires C, 77·4; H, 9·75%). *Active hydrogen* (Zerewitinoff): The ether (76 mg.) evolved 13·4 c.c. of methane (after heating to 90°) at 19°/760 mm. (0·9 active hydrogen atom per mol.).

Propenylethynylcarbinol from 3-Acetoxyhex-4-en-1-yne.—A solution of 3-acetoxyhex-4-en-1-yne (6 g.; Jones and McCombie, J., 1942, 733) in methyl alcohol (7 c.c.) was refluxed for 6 hours in the presence of anhydrous potassium carbonate (3 g.). Isolation of the product with ether in the usual manner gave propenylethynylcarbinol (3·1 g.), b. p. 86°/50 mm., $n_D^{19°}$ 1·4664. The *α-naphthylurethane* crystallised in needles from light petroleum (b. p. 60—80°) and had m. p. 98—99·5°, undepressed on admixture with a specimen made from an authentic sample of carbinol (Found: N, 5·35. $C_{17}H_{15}O_2N$ requires N, 5·3%).

2 : 9-Diethoxydeca-3 : 7-dien-5-yne (IV; R = OEt).—To a solution of concentrated sulphuric acid (2 g.) in alcohol (40 c.c.), deca-2 : 8-dien-5-yne-4 : 7-diol (3 g.; Heilbron, Jones, and Raphael, J., 1943, 268) was added, and the mixture was kept at about 20° for 5 days. Isolation by means of ether gave the *ether* (IV; R = OEt) (2·3 g.), b. p. 93—95°/0·03 mm., $n_D^{16°}$ 1·4991 (Found: C, 75·65; H, 10·05. $C_{14}H_{22}O_2$ requires C, 75·7; H, 9·9%).

Di-2-(hex-3-en-5-ynyl) Ether (V).—(*a*) A mixture of propenylethynylcarbinol (51 g.) and sulphuric acid (2 c.c.; 2N) was heated in a distilling flask at 80°/50 mm. for 10 minutes and then distilled in an atmosphere of nitrogen at the same pressure. The high-boiling fraction obtained after removal of water and hex-3-en-5-yn-2-ol was redistilled through a 24-cm. Dufton column, giving *di-2-(hex-3-en-5-ynyl) ether* (25 g.) as a colourless oil, b. p. 72—74°/5 mm., $n_D^{20·5°}$ 1·4950 (Found: C, 82·8; H, 8·0. $C_{12}H_{14}O$ requires C, 82·75; H, 8·05%).

(*b*) Repetition of the above procedure with hex-3-en-5-yn-2-ol (10 g.) gave the ether (2·5 g.), b. p. 66—68°/3·5 mm., $n_D^{16°}$ 1·4977.

Di-2-(n-hexyl) Ether.—The above ether (14·2 g.) in ethyl acetate (200 c.c.) was completely hydrogenated in the presence of platinic oxide (40 mg.). Isolation of the product in the usual manner gave di-2-(*n*-hexyl) ether (13·5 g.), b. p. 95—97°/22 mm., $n_D^{22°}$ 1·4183 (Found: C, 77·25; H, 13·95. Calc. for $C_{12}H_{26}O$: C, 77·35; H, 14·05%) (Vernimmen, *Bull. Soc. chim. Belg.*, 1924, **33**, 96, gives b. p. 200°/760 mm., $n_D^{20°}$ 1·4152).

3-n-*Butoxyhex-4-en-1-yne.*—A solution of crotonaldehyde (140 g.) in ether (200 c.c.) was added during 1½ hours to a liquid ammonia solution (1·5 l.) of sodium acetylide, prepared from sodium (47 g.) as described below. After an hour's stirring, *n*-butyl bromide (274 g.) in ether (150 c.c.) was added during 1½ hours, followed after a further 1½ hours by ammonium chloride (120 g.), and the solvent was allowed to evaporate off overnight. The product, isolated with ether, was distilled, and the portion with b. p. above 62°/145 mm. was redistilled through a 24-cm. Dufton column. In this way there were obtained: (i) propenylethynylcarbinol (67 g.), b. p. 74—76°/30 mm. (α-naphthylurethane, m. p. and mixed m. p., 98—99°); (ii) 3-n-*butoxyhex-4-en-1-yne* (12 g.), a colourless liquid with a pleasant odour, b. p. 88—89°/30 mm., $n_D^{19·5°}$ 1·4453 (Found: C, 79·2; H, 10·8. $C_{10}H_{16}O$ requires C, 78·9; H, 10·6%). The ether shows no appreciable light absorption in the range 2200—4000 A. *Active hydrogen* (Zerewitinoff): The ether (81 mg.) evolved 12·5 c.c. of methane at 25°/772 mm. (after heating to 90°) (1·0 active hydrogen atom per mol.).

Improved Preparation of Propenylethynylcarbinol.—The reaction vessel consisted of a 3-necked, 10-l. flask set up in an alcohol and "dry-ice" cooling bath. The flask was fitted with an efficient mercury-seal stirrer, a gas inlet leading nearly to the bottom of the flask, thermometer, and a gas outlet tube packed with soda-lime. The solid materials were introduced by removing the stopper from one of the necks of the flask, and the liquid (crotonaldehyde in ether) by means of a dropping-funnel temporarily inserted in one of the necks.

About 6 l. of liquid ammonia were run into the reaction flask, the latter being cooled to — 40°; then finely powdered hydrated ferric nitrate (3 g.) was added, and the mixture stirred for a few minutes to effect solution, which was followed by addition of sodium (10 g.). The mixture was stirred until the colour changed from blue to a brownish-black.

In some cases it may be necessary to pass dry air through the mixture in order completely to remove the blue colour. At this point a slow stream of dry nitrogen was introduced, and the bath temperature was raised by addition of alcohol until the internal temperature reached — 35°. Sodium (345 g.), cut in cubes of about ½ inch size, was added piecemeal into the mixture, and stirring continued until the colour changed from a deep blue to a light grey, indicating conversion of sodium into sodamide (25—50 minutes). While the temperature was kept at about — 35°, acetylene, purified by passage through a tower (90 × 3 cm.) of silica gel and by bubbling through concentrated sulphuric acid, was introduced with the nitrogen at a rate of about 3 l./min. After 2—2½ hours the mixture again turned black, corresponding to the completion of the formation of sodium acetylide (cf. Kreimeier, U.S.P. 2,106,181). The acetylene flow was then reduced to 50—100 c.c./min., and a solution of redistilled crotonaldehyde (1050 g.) in about twice its volume of dry ether added over a period of 4 hours, the temperature being maintained at about — 32°. The mixture was stirred for a further 3 hours. At this point the reaction was stopped by the gradual addition of ammonium chloride (825 g.), a considerable amount of heat being evolved in this process. The mixture was stirred for a further 30 minutes to complete the decomposition of the sodio-compound. The reaction flask was then removed from the cooling bath and the ammonia allowed to evaporate off overnight, the mixture being stirred gently throughout. The suspension of salt thus obtained was filtered off at the pump, and the solid washed thoroughly with ether. Evaporation of the ethereal solution gave a residue which on distillation in nitrogen gave propenylethynylcarbinol (1085 g.; 75% yield based on the crotonaldehyde), b. p. 74—75°/30 mm., $n_D^{21°}$ 1·4645.

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22. *Studies in the Polyene Series. Part XIX. The Semihydrogenation of Ethynylcarbinols derived from αβ-Unsaturated Aldehydes, and the Anionotropic Rearrangements of the Resulting Vinylcarbinols.**

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Partial hydrogenation of the acetylenic linkage of propenylethynylcarbinol (I) and of two related ethynylcarbinols proceeds smoothly with a 0·3% palladium–calcium carbonate catalyst. The resulting vinylcarbinols are much more readily isomerised by acids than the parent ethynylcarbinols; for instance, whereas vinylethynylcarbinol is unaffected by 25% sulphuric acid, divinylcarbinol is isomerised merely by shaking with 1% acid at room temperature. The butadienylcarbinols (VI, VII, and VIII) resulting from these rearrangements exhibit ultra-violet absorption characteristic of conjugated dienes, and although they add readily to maleic anhydride they give rise to lactonic acids (*e.g.*, X), containing a highly stable lactone ring.

The electron-repelling properties of the methyl group appear to be of paramount importance in determining the nature of the isomerisation product of propenylvinylcarbinol, which is shown to be the secondary alcohol, hexa-3 : 5-dien-2-ol (VI), since it yields methylbutylcarbinol on complete hydrogenation. The rearrangement of divinylcarbinol is unambiguous, and that of *iso*propenylvinylcarbinol probably leads to 2-methylpenta-2 : 4-dien-1-ol (VIII).

The partial reduction of acetylenic linkages has been extensively investigated, particularly during the past twenty years, and Campbell and Campbell (*Chem. Reviews*, 1942, **31**, 77) have surveyed the catalytic, chemical, and electrochemical methods which have all been employed. In general, catalytic hydrogenation is the most convenient and effective method, and palladium catalysts (usually in the colloidal state) are the most selective, but with an iron catalyst of the Raney type (Paul and Hilly, *Bull. Soc. chim.*, 1939, **6**, 218; Thompson and Wyatt, *J. Amer. Chem. Soc.*, 1940, **62**, 2555, and later papers) hydrogenation is reported to cease at the olefin stage. Although the ethylenic compounds often hydrogenate as rapidly as or even more rapidly than the original acetylenic compounds and no appreciable discontinuity in the rate of uptake of hydrogen can therefore be discerned, it is nevertheless possible to obtain excellent yields of the required semihydrogenation products by interrupting the reaction at the appropriate stage. It has been suggested (Farkas, *Trans. Faraday Soc.*, 1939, **35**, 909) that selective adsorption of the acetylenic compound on the catalyst is responsible for the stepwise reduction.

The partial reduction of propenylethynylcarbinol (I) to propenylvinylcarbinol (II) in aqueous suspension by use of Bourguel's colloidal palladium catalyst was originally reported by Lespieau and Lombard (*Bull. Soc. chim.*, 1935, **2**, 372), who noted an acceleration in the rate of hydrogenation after one mol. of hydrogen had been absorbed and a diminution in rate after 2 mols. had been taken up. We have observed a similar behaviour with both palladium–norit and palladium–calcium carbonate catalysts but, as has usually been the experience of other workers with numerous acetylenic compounds, with a platinic oxide catalyst no discontinuity in the rate of hydrogenation is discernible. With propenylethynylcarbinol (I) the rate of hydrogenation is so rapid

(I.) $CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH$ $\qquad$ $CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CH{:}CH_2$ (II.)

that it is most convenient to employ a palladium–calcium carbonate catalyst containing only 0·3% of palladium. The hydrogenation can readily be interrupted so that reduction proceeds exclusively at the acetylenic linkage,

* Patent application pending.

giving propenylvinylcarbinol (II) in 90% yield, its homogeneity being proved by fractionation through a column of high efficiency, whereafter no appreciable variation in refractive index is observed. The carbinol contains one active hydrogen atom (Zerewitinoff), it gives no trace of a silver salt with ammoniacal silver nitrate, and it is readily characterised as the *α-naphthylurethane*, m. p. 93·5—94·5°.

In a similar manner, divinylcarbinol (III) (*α-naphthylurethane*) can be prepared in 70% yield from vinylethynylcarbinol, and *iso*propenylethynylcarbinol gives iso*propenylvinylcarbinol* (IV) (*α-naphthylurethane*) in 80% yield. As would be expected, none of the carbinols (II, III, and IV) exhibits any light absorption of

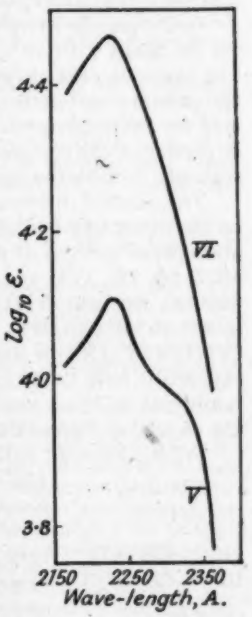
(III.) CH_2:CH·CH(OH)·CH:CH_2 CH_2:CMe·CH(OH)·CH:CH_2 (IV.)

appreciable intensity in the 2200—4000 A. range.

The anionotropic rearrangement of acetylenylcarbinols and glycols derived from αβ-unsaturated carbonyl compounds, first observed (Jones and McCombie, J., 1943, 261) with propenylethynylcarbinol (I) which gives (V), has been extensively investigated (J., 1943—1945; Parts VIII—XVIII inclusive), and an examination of the behaviour of the vinylcarbinols (*e.g.*, II, III, and IV) represents a logical continuation of this study. When propenylvinylcarbinol (II) is shaken at room temperature for two hours with 1% sulphuric acid an 80% yield of *hexa*-3 : 5-*dien*-2-*ol* (*methyl*-1-*butadienylcarbinol*) (VI) is obtained. The yield diminishes

(V.) CH_3·CH(OH)·CH:CH·C:CH CH_3·CH(OH)·CH:CH·CH:CH_2 (VI.)

with increasing concentrations of acid; *e.g.*, 2·5% acid for 4½ hours gives only a 60% yield, and with 5% acid at 90° for 20 minutes the product is a pale yellow viscous liquid which fails to distil up to 140°/4 mm. The striking difference in the ease of rearrangement of (I) and (II) [(I) is only isomerised to the extent of 5% with 2·5% acid during one hour at 20°] must clearly be related to the relative electronic properties of the acetylenic and the ethylenic bonds. Comparison of the strengths of corresponding pairs of carboxylic acids (Dippy, *Chem. Reviews*, 1939, **25**, 180), *viz.*, CH_3·CH:CH·CO_2H, 10^5K = 2·03, CH_3·C:C·CO_2H, 10^5K = 222·8, clearly demonstrates the greater ability of the ethylenic bond to release electrons, which must be the main factor responsible for the superior mobility of the system present in propenylvinylcarbinol. Such electron release will clearly facilitate the formation of the oxonium ion which has been postulated (Braude and Jones, J., 1944, 436) as the principal intermediate in the isomerisation of propenylethynylcarbinol.



The rearrangement product contains one active hydrogen atom (Zerewitinoff), it gives an *α-naphthylurethane* and a crystalline adduct (see below) with maleic anhydride, and its ultra-violet absorption (Fig. and Table) is characteristic of the conjugated diene system. This light absorption is about twice as intense as that of the related vinylethynylcarbinol (V), and although the locations of the maxima are identical, the inflexion, typical of the conjugated enyne chromophore, is absent from the spectrum of (VI) (see Fig.).

	$\lambda_{max.}$, A.	$\varepsilon_{max.}$		$\lambda_{max.}$, A.	$\varepsilon_{max.}$
Hexa-3 : 5-dien-2-ol (VI)	2230	28,000	Piperylene [1]	2235	23,000
Penta-2 : 4-dien-1-ol (VII)	2230	25,000	$\Delta^{2:4}$-Hexadiene [1]	2270	22,500
2-Methylpenta-2 : 4-dien-1-ol (VIII)	2285	25,500	Hex-3-en-5-yn-2-ol [2] (V)	2230	13,500
				*2300	9,500

* Inflexion.

[1] Booker, Evans, and Gillam, J., 1940, 1453. [2] Jones and McCombie, *loc. cit.*

The rearrangement of (II) might conceivably give rise either to the primary carbinol, sorbyl alcohol, or to the secondary dienol (VI), both of which would be expected to show the properties referred to above. The constants quoted for sorbyl alcohol in the literature (m. p. 30·5—31·5°, b. p. 76—77°/12 mm.; Reichstein, Ammann, and Trivelli, *Helv. Chim. Acta*, 1932, **15**, 261), however, are quite different from those of the actual isomerisation product, and the formulation of the latter as (VI), which is strongly supported by the exact location of the absorption maximum, referred to again later, is conclusively proved by its complete hydrogenation to methylbutylcarbinol. The greater electron-repelling tendency of the methyl group as compared with that of the hydrogen atom must be the controlling factor in determining the direction of isomerisation in this case : CH_3→CH:CH·CH(OH)·CH:CH—H.

Theoretically, the partial reduction of conjugated vinylacetylenes can proceed in three ways. 1 : 2-Addition, *i.e.*, semihydrogenation of the acetylenic linkage, leading to a conjugated diene; 1 : 4-addition, giving an allene; and 3 : 4-addition, resulting in the formation of a simple acetylene. Although many cases of successful 1 : 2-addition are reported in the literature, these are usually supported only by evidence of a qualitative nature and the quantitative selectivity of any particular catalyst cannot readily be assessed. Palladium catalysts, however, would appear to be the most efficacious, and consequently the partial reduction of hex-3-en-5-yn-2-ol (V) was examined by employing a palladium–calcium carbonate catalyst. The hydrogenation was stopped at the appropriate stage, and by careful fractionation a 40% yield of hexa-3 : 5-dien-2-ol (VI) was obtained. The light absorption and other properties of this product were identical with those of the carbinol obtained by the alternative route. There is a little doubt that 1 : 2-hydrogenation occurs mainly if not almost ex-

clusively in this case, since the dienol actually formed more than 60% of the distillable product; much undistillable material was obtained, probably formed from the somewhat sensitive dienol during the protracted fractionation.

In contrast to the behaviour of vinylethynylcarbinol, which is unaffected by treatment with 25% sulphuric acid (Jones and McCombie, *loc. cit.*), divinylcarbinol (III) is isomerised to *penta*-2 : 4-*dien*-1-*ol* (VII) (*α-naphthylurethane*) in 20% yield by shaking with 1% sulphuric acid for 24 hours. The rearrangement in this case is accompanied by the formation of much low b. p. material which may be of the methyldihydrofuran or the

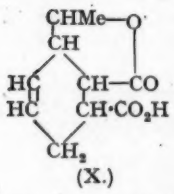
(VII.) $CH_2(OH)\cdot CH{:}CH\cdot CH{:}CH_2$ $CH_2(OH)\cdot CMe{:}CH\cdot CH{:}CH_2$ (VIII.) $CH_2{:}CMe\cdot CH{:}CH\cdot CH_2\cdot OH$ (IX.)

dihydropyran type. Unfortunately, the relative inaccessibility of vinylethynylcarbinol and hence of divinylcarbinol, precluded the possibility of more detailed investigations of the isomerisation conditions and of these by-products. The butadienylcarbinol (VII) gives *n*-amyl alcohol on complete hydrogenation, it exhibits high-intensity light absorption (Table), and readily forms an adduct (see below) with maleic anhydride.

*iso*Propenylethynylcarbinol, like the closely related vinylethynylcarbinol, is not isomerised even on shaking for 24 hours with 25% sulphuric acid, but this is again by no means true of its semihydrogenation product. The isomerisation of *iso*propenylvinylcarbinol (IV) could conceivably proceed in either of two directions, giving the primary carbinols (VIII) or (IX). The product obtained in 45% yield on shaking (IV) with 2% sulphuric acid for 24 hours appears to consist essentially of 2-*methylpenta*-2 : 4-*dien*-1-*ol* (VIII), since 2-methylpentan-1-ol is produced on complete hydrogenation. The carbinol absorbs strongly in the ultra-violet (Table), and in spite of a notable tendency to polymerise, it gives an *α-naphthylurethane* and a maleic anhydride *adduct* (see below).

The marked differences in location of absorption maxima between (VIII) on the one hand, and (VI) and (VII) on the other (see Table), are in accord with observations on the effect of the degree of alkyl substitution on the absorption spectra of diene systems. According to the generalisations of Woodward (*J. Amer. Chem. Soc.*, 1942, **64**, 72), (VI) and (VII) and piperylene should, as monosubstituted butadienes, exhibit maxima at about 2220 A., whereas (VIII) and $\Delta^{2:4}$-hexadiene, being disubstituted butadienes, should show maximal absorption in the vicinity of 2270 A. The carbinol (IX) is also a disubstituted butadiene, and no differentiation between (VIII) and (IX) on the basis of the location of the absorption maximum is possible. Sorbyl alcohol, which originally had to be considered as a possible rearrangement product of (II), would be expected to absorb mainly at 2270 A., but von Euler, Karrer, Klussmann, and Morf (*Helv. Chim. Acta*, 1932, **15**, 502) do not quote the exact location of the absorption maximum.

When hexa-3 : 5-dien-2-ol (VI) reacts with maleic anhydride in benzene solution an adduct, m. p. 157—158°, is produced which is formulated as the *γ-lactone* of 3-*α-hydroxyethyl*-Δ^4-cyclo*hexene*-1 : 2-*dicarboxylic acid* (X). Similarly constituted lactonic *acids* are obtained from carbinols (VII) and (VIII). The lactonic acid (X) fails to show any high-intensity absorption in the ultra-violet in the range 2200—4000 A., catalytic hydrogenation indicates the presence of one ethylenic linkage, on heating with *p*-toluidine it forms a *mono*-p-*toluidide*, and with diazomethane it gives a *monomethyl* ester. The lactone ring is extremely stable, as in phthalide and related compounds, and (X) is recovered unchanged after being heated at 50° with methyl sulphate and 35% potassium hydroxide. No analogous case of the immediate formation of lactonic acids by Diels–Alder addition reactions is mentioned in the review by Norton (*Chem. Reviews*, 1942, **31**, 319), but the anil of ethylhexenal is reported to react in its isomeric form ($CHEt{:}CH\cdot CEt{:}CH\cdot NHPh$) with maleic anhydride, giving a monobasic acid containing a five-membered lactam ring (Snyder, Hasbrouck, and Richardson, *J. Amer. Chem. Soc.*, 1939, **60**, 3558).



(X.)

Experimental.

(Absorption spectra were determined in alcoholic solutions.)

Propenylvinylcarbinol (II).—A solution of propenylethynylcarbinol (250 g., preceding paper) in ethyl acetate (400 c.c.) was shaken with hydrogen in the presence of palladium–calcium carbonate (20 g.; 0·3% Pd). Absorption of hydrogen was extremely rapid, and after 62 l. had been absorbed the catalyst was filtered off, and the solvent evaporated off through a column. Distillation of the residual oil through a column * containing a 50 × 1·5 cm. section packed with single-turn glass helices gave propenylvinylcarbinol (227 g.), b. p. 86—87°/100 mm., 71°/50 mm., 60—62°/28 mm., $n_D^{19°}$ 1·4501 (Lespieau and Lombard, *loc. cit.*, give b. p. 140°, 52°/13 mm., $n_D^{24°}$ 1·4482) (Found: C, 73·8; H, 10·25. Calc. for $C_6H_{10}O$: C, 73·4; H, 10·25%). *Active hydrogen* (Zerewitinoff): At 16°/772 mm. the carbinol (99·5 mg.) evolved 22·7 c.c. of methane, equivalent to 0·95 active hydrogen atom per mol. The *α-naphthylurethane* separated from light petroleum (b. p. 60—80°) in needles, m. p. 93·5—94·5° (Found: N, 5·35. $C_{17}H_{17}O_2N$ requires N, 5·25%).

Divinylcarbinol (III).—A solution of vinylethynylcarbinol (25 g.; Jones and McCombie, J., 1942, 733) in ether (100 c.c.) was hydrogenated, palladium–calcium carbonate (3 g.; 0·3% Pd) being used as catalyst. The experiment was interrupted after 9 l. of hydrogen had been absorbed and yielded divinylcarbinol (17·2 g.), a colourless liquid with a somewhat pungent odour, b. p. 64—66°/100 mm., $n_D^{17°}$ 1·4400 (Lespieau and Lombard, *loc. cit.*, give b. p. 114·5—116°, $n_D^{19°}$ 1·4452). The *α-naphthylurethane* separated from aqueous methyl alcohol as felted needles, m. p. 100—101° (Found: N, 5·45. $C_{16}H_{15}O_2N$ requires N, 5·55%).

*iso*Propenylvinylcarbinol (IV).—*iso*Propenylethynylcarbinol (20 g.; for preparation, see below) was hydrogenated in methyl acetate (100 c.c.) with palladium–calcium carbonate (2 g.; 0·3% Pd) as catalyst. The experiment was interrupted after 4·7 l. of hydrogen had been taken up, and fractionation of the product yielded *iso*propenylvinylcarbinol (16·5 g.), b. p. 66°/50 mm., $n_D^{18°}$ 1·4530 (Found: C, 73·6; H, 10·1. $C_6H_{10}O$ requires C, 73·4; H, 10·25%). The *α-naphthylurethane* crystallised from light petroleum (b. p. 40—60°) in long, matted needles, m. p. 88—89° (Found: N, 5·4. $C_{17}H_{17}O_2N$ requires N, 5·25%).

* This column has an efficiency of twelve theoretical plates when tested with a CCl_4–C_6H_6 mixture.

Hexa-3 : 5-dien-2-ol (VI).—(*a*) A mixture of propenylvinylcarbinol (210 g.) and sulphuric acid (550 c.c.; 1% w/v) together with a little quinol, was shaken under nitrogen at 20° for 2 hours. Isolation of the product by ethereal extraction followed by two distillations of the residual oil gave *hexa-3 : 5-dien-2-ol* (172 g.) as a colourless oil, b. p. 67—68°/26 mm., $n_D^{19°}$ 1·4810 (Found: C, 73·75; H, 10·2. $C_6H_{10}O$ requires C, 73·4; H, 10·25%). Some resin was formed during the distillation. *Active hydrogen* (Zerewitinoff): The carbinol (100 mg.) evolved 24·4 c.c. of methane at 12°/752 mm. (0·95 active hydrogen atom per mol.). The *α-naphthylurethane* crystallised from light petroleum (b. p. 60—80°) in clusters of leaflets, m. p. 86·5—87·5° (Found: N, 5·4. $C_{17}H_{17}O_2N$ requires N, 5·25%).

(*b*) Hex-3-en-5-yn-2-ol (150 g.; Jones and McCombie, J., 1943, 261) was hydrogenated in ethyl acetate (400 c.c.) by using a palladium–calcium carbonate catalyst (15 g.; 0·3% Pd), the experiment being interrupted when 34·5 l. of gas had been absorbed. The catalyst and solvent were eliminated and the residue was fractionated through a column containing a 50 × 1·5 cm. section packed with single-turn glass helices. The many fractions collected were readily divided into two main portions: (i) B. p. 65—73°/35 mm. (35 g.), $n_D^{17°}$ 1·4469—1·4740; (ii) hexa-3 : 5-dien-2-ol (61 g.), b. p. 73—75°/35 mm. $n_D^{19°}$ 1·4813. There was a cousiderable resinous residue. Portion (ii) showed light absorption identical with that of the material obtained under (*a*), and the same α-naphthylurethane was obtained.

Methylbutylcarbinol and Methyl Butyl Ketone.—Hexa-3 : 5-dien-2-ol (7 g.) in methyl acetate (85 g.) was hydrogenated completely by using platinic oxide (300 mg.) as catalyst. This procedure gave methylbutylcarbinol (6 g.), b. p. 135—139°, $n_D^{18°}$ 1·4130 (lit., b. p. 135—137°, $n_D^{18°}$ 1·4135), which was oxidised to methyl butyl ketone, the 2 : 4-dinitrophenylhydrazone of which had m. p. 108·5° (after chromatographic purification), undepressed on admixture with an authentic specimen (Allen, *J. Amer. Chem. Soc.*, 1930, **52**, 2957, gives m. p. 106°).

Penta-2 : 4-dien-1-ol (VII).—Divinylcarbinol (11·7 g.) was shaken with sulphuric acid (100 c.c.; 1% w/v) under nitrogen at 20° for 24 hours. Distillation of the product isolated with ether gave 3 fractions: (i) B. p. up to 75°/120 mm. (2·5 g.); (ii) b. p. 75—90°/120 mm. (1 g.), $n_D^{19°}$ 1·4443; (iii) b. p. 90—102°/120 mm. (3 g.), $n_D^{19°}$ 1·4823, and a pale yellow viscous residue. Redistillation of (iii) gave *penta-2 : 4-dien-1-ol* (2·5 g.) as a colourless liquid with a sweetish odour, b. p. 95—97°/100 mm., $n_D^{18°}$ 1·4902 (Found: C, 71·65; H, 9·9. C_5H_8O requires C, 71·45; H, 9·6%). The carbinol, like hexa-3 : 5-dien-2-ol, polymerises to a clear elastic material on standing. The *α-naphthylurethane* crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 97·5° (Found: N, 5·55. $C_{16}H_{15}O_2N$ requires N, 5·55%).

n-Amyl Alcohol.—The above carbinol (1·8 g.) was completely hydrogenated in methyl acetate (50 c.c.) by means of a platinic oxide catalyst and gave *n*-amyl alcohol (0·75 g.), b. p. 134—138° (α-naphthylurethane, m. p. 68°, undepressed on admixture with an authentic specimen).

2-Methylpenta-2 : 4-dien-1-ol (VIII).—A mixture of *iso*propenylvinylcarbinol (10 g.) and sulphuric acid (100 c.c.; 2% w/v) together with a trace of quinol was shaken under nitrogen at 20° for 24 hours. After saturation with salt the product was isolated with ether, giving *2-methylpenta-2 : 4-dien-1-ol* (4·6 g.), b. p. 97—99°/50 mm., 72—74°/15 mm., $n_D^{19·5°}$ 1·5001 (Found: C, 73·25; H, 10·1. $C_6H_{10}O$ requires C, 73·4; H, 10·25%). Much rubbery polymer was formed during the preparation at 20° of the *α-naphthylurethane*, which crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 59—60° (Found: N, 5·2. $C_{17}H_{17}O_2N$ requires N, 5·25%).

2-Methylpentan-1-ol.—The above dienol (3 g.) was fully hydrogenated in methyl acetate (50 c.c.) with platinic oxide (100 mg.) as catalyst and, after careful removal of solvent through a column, gave 2-methylpentan-1-ol (2·4 g.), b. p. 146—151°/776 mm., $n_D^{15·5°}$ 1·4238 (cf. $n_D^{25°}$ 1·4180 given by Norris and Cortese, *J. Amer. Chem. Soc.*, 1927, **49**, 2644; $n_D^{19°}$ 1·4182 by Przewalski, *Chem. Zentr.*, 1909, II, 794; $n_D^{19°}$ 1·4230 by Terentjew, *Bull. Soc. chim.*, 1924, **35**, 1152, and the values for the isomeric 4-methylpentan-1-ol: $n_D^{20°}$ 1·4134, Norris and Cortese, *loc. cit.*; $n_D^{20°}$ 1·4142, Longinow, *Chem. Zentr.*, 1916, I, 1054). The crude α-naphthylurethane had m. p. 63—67°, but after several recrystallisations from light petroleum (b. p. 40—60°) it formed long needles, m. p. 79—80° (Found: N, 5·25. Calc. for $C_{17}H_{21}O_2N$: N, 5·15%) (Magnani and McElvain, *J. Amer. Chem. Soc.*, 1938, **60**, 819, give m. p. 75—76° for the derivative of 2-methylpentan-1-ol, and Huston and Agett, *J. Org. Chem.*, 1941, **6**, 128, give m. p. 60° for the derivative of the 4-methyl isomer).

γ-Lactone of 3-α-Hydroxyethyl-Δ⁴-cyclohexene-1 : 2-dicarboxylic Acid (X).—A mixture of hexa-3 : 5-dien-2-ol (5 g.), purified maleic anhydride (5 g.), and benzene (50 c.c.) was heated to about 80° for a few minutes to effect solution and then set aside for 3 days at 20°. In alcoholic solution the addition reaction is much more rapid. Crystallisation of the separated solid from benzene or water gave the above lactonic *acid* (5·5 g.) as prismatic needles, m. p. 157—158° (Found: C, 61·0; H, 6·05. $C_{10}H_{14}O_4$ requires C, 61·2; H, 6·15%). The *methyl* ester, prepared by using diazomethane in ethereal solution, crystallised from water in flat needles, m. p. 140·5—141·5° (Found: C, 63·1; H, 6·75. $C_{11}H_{16}O_4$ requires C, 62·85; H, 6·7%). Heating the lactone with *p*-toluidine at 220° for 20 minutes gave the p-*toluidide* as leaflets from aqueous alcohol, m. p. 172° (Found: C, 71·5; H, 6·9. $C_{17}H_{19}O_3N$ requires C, 71·55; H, 6·7%).

γ-Lactone of 3-Hydroxymethyl-Δ⁴-cyclohexene-1 : 2-dicarboxylic Acid.—A warm solution of penta-2 : 4-dien-1-ol (0·8 g.) and purified maleic anhydride (1 g.) in benzene (8 c.c.) was set aside at 20° and a mass of crystals separated after 3 hours. Recrystallisation of these from water gave the lactonic *acid* as large prisms, m. p. 175—176° (Found: C, 59·55; H, 5·65. $C_9H_{10}O_4$ requires C, 59·35; H, 5·5%).

γ-Lactone of 3-Hydroxymethyl-3-methyl-Δ⁴-cyclohexene-1 : 2-dicarboxylic Acid.—The crystals which separated on keeping a solution of 2-methylpenta-2 : 4-dien-1-ol (3·5 g.) and purified maleic anhydride (3·5 g.) in dry benzene (8 c.c.) containing a trace of quinol at 20°, were recrystallised from water or sublimed at 115° (bath temp.)/10^{-4} mm., giving the lactonic *acid* (2·5 g.) as rectangular plates, m. p. 181—182° (Found: C, 61·25; H, 6·25. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·15%). The original benzene mother-liquors contained much rubbery polymeric material.

α-Methylacraldehyde (cf. D.R.P. 482,839; B.PP. 286,602, 457,174; Shriner and Sharp, *J. Amer. Chem. Soc.*, 1940, **62**, 2245; Hearne, Tamele, and Converse, *Ind. Eng. Chem.*, 1941, **33**, 805).—α-Methylallyl alcohol (46 g.) was added dropwise during 2 hours to a stirred suspension of selenium dioxide (35 g., freshly sublimed in oxygen) in dioxan (80 g.). The mixture was heated under gentle reflux during the addition in such a manner that the temperature at the head of the 24-cm. Dufton column fitted to the flask did not exceed 90°. When the addition was complete, more selenium dioxide (5 g.) was added, and heating was continued until the b. p. of the distillate rose above 90°. Some 50—75 c.c. of distillate were collected. The distillates from two such experiments were combined and carefully fractionated through a column packed with a 50 × 1·5 cm. section of single-turn glass helices. The fraction with b. p. 63·5—64° was dried, and on redistillation yielded α-methylacraldehyde (30 g.), b. p. 67—69°/770 mm., $n_D^{18°}$ 1·4166.

iso-Propenylethynylcarbinol.—A solution of α-methylacraldehyde (30 g.) in ether (50 c.c.) was added to a stirred solution of sodium acetylide (from sodium 8·5 g. *via* sodamide made *in situ* according to Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120) in liquid ammonia (500 c.c.). Stirring was continued for 2 hours, ammonium chloride added, and the solvent allowed to evaporate off overnight. Isolation in the usual manner gave *iso*propenylethynylcarbinol (25 g.), b. p. 74°/50 mm., $n_D^{18·5°}$ 1·4629 (Kreimeier, U.S.P. 2,106,181, gives b. p. 141—144°, $n_D^{25°}$ 1·4589). The *α-naphthylurethane* crystallised from light petroleum (b. p. 40—60°) in long needles, m. p. 99—100° (Found: N, 5·2. $C_{17}H_{15}O_2N$ requires N, 5·3%).

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23. *Studies in the Polyene Series. Part XX. The Formation of Ethers and Esters from Propenylvinylcarbinol and Related Compounds, and the Simultaneous Rearrangements.**

By I. M. Heilbron, E. R. H. Jones, J. T. McCombie, and B. C. L. Weedon.

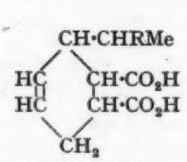
Treatment of propenylvinylcarbinol (III; R = OH) with alcohols and sulphuric acid gives ethers of hexa-3 : 5-dien-2-ol (IV; R = OH) which exhibit high-intensity ultra-violet absorption characteristic of conjugated dienes and, unlike the corresponding carbinols, form normal adducts with maleic anhydride. The acetate (III; R = OAc), prepared with acetic anhydride and pyridine in the cold, is isomerised to the acetate (IV; R = OAc) with acetic anhydride at 100°. This also gives a normal Diels–Alder adduct, but when either the anhydride or the corresponding acid (V; R = OAc) is hydrolysed with boiling hydrochloric acid a lactonic acid (VI) is produced, which is probably a stereoisomer of that prepared directly from the dienol (Part XIX).

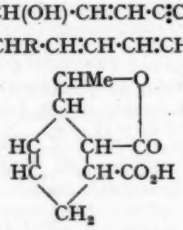
The behaviour of divinylcarbinol (VII; R = OH) provides a striking contrast in that no rearrangement accompanies the formation of either the methyl ether or the acetyl derivative, even when the latter is prepared in boiling acetic anhydride.

The rearrangement of propenylethynylcarbinol (I) with concentrated sulphuric acid in the presence of alcohols has been shown (Part XVIII) to result in the formation of ethers of the conjugated vinylacetylenylcarbinol (II). The enhanced mobility of the anionotropic system of propenylvinylcarbinol (III; R = OH) when compared with that of (I) suggested that in this case ether formation and the accompanying rearrangement would be easy to effect. When (III; R = OH) is treated with alcoholic sulphuric acid at room temperature

(I.) $CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH$ $\qquad$ $CH_3{\cdot}CH(OH){\cdot}CH{:}CH{\cdot}C{\vdots}CH$ (II.)

(III.) $CH_3{\cdot}CH{:}CH{\cdot}CHR{\cdot}CH{:}CH_2$ $\qquad$ $CH_3{\cdot}CHR{\cdot}CH{:}CH{\cdot}CH{:}CH_2$ (IV.)

(V.) 

(VI.) 

the *ether* (IV; R = OEt), is obtained in about 60% yield, and the 2-*methoxy*-analogue can be prepared in a similar manner. Both ethers are probably formed in practically theoretical yields but losses occur during isolation owing to their high volatility. With ethylene chlorohydrin and sulphuric acid 2-β-*chloroethoxyhexa*-3 : 5-*diene* (IV; R = $CH_2Cl{\cdot}CH_2{\cdot}O$) is obtained from (III; R = OH). These diene-ethers all exhibit high-intensity light absorption in the ultra-violet (Table) and from the ethyl ether and maleic anhydride, a

	$\lambda_{max.}$, A.	$\varepsilon_{max.}$
2-Ethoxyhexa-3 : 5-diene (IV; R = OEt)	2230	26,000
2-Methoxyhexa-3 : 5-diene (IV; R = OMe)	2235	30,000
2-β-Chloroethoxyhexa-3 : 5-diene (IV; R = $CH_2Cl{\cdot}CH_2O$)	2280	34,000
2-Acetoxyhexa-3 : 5-diene (IV; R = OAc)	2235	27,500
Hexa-3 : 5-dien-2-ol [1] (IV; R = OH)	2230	27,500
Hydrogen phthalate of (IV; R = OH) *	2230	39,500

[1] Part XIX. * In N-alcoholic KOH.

normal adduct, the *anhydride* of 3-α-*ethoxyethyl*-Δ^4-cyclo*hexene*-1 : 2-*dicarboxylic acid*, giving the *acid* (V; R = OEt) on refluxing with water, is formed. Similarly the *acid* (V; R = OMe) and the corresponding *anhydride* are obtained from the methyl ether.

In spite of the ease of rearrangement of propenylvinylcarbinol (III; R = OH), when treated in the cold with acetic anhydride in the presence of pyridine it is quantitatively converted into the *acetate* (III; R = OAc), without isomerisation. The latter remains unchanged after heating in benzonitrile at 100° for 18 hours, but in acetic anhydride at the same temperature it undergoes isomerisation † to 2-*acetoxyhexa*-3 : 5-*diene* (IV; R = OAc) (for light absorption, see Table), which can also be prepared directly from the carbinol (III; R = OH) in this way. This rearranged acetate (IV; R = OAc) is best obtained, however, by acetylation of the isomerised carbinol (IV; R = OH) in the cold with acetic anhydride in the presence of pyridine, for in many acetylation experiments, particularly those carried out at elevated temperatures, variable quantities of high-boiling products were produced. Nazarov (*Bull. Acad. Sci. U.R.S.S.*, 1938, 695) observed ether formation accompanying the acetylation of a vinylacetylenylcarbinol, but with neither propenylvinylcarbinol nor its isomer could any homogeneous C_{12} ether, corresponding to that described in Part XVIII, be isolated, almost certainly owing to the greater ease with which polymerisation reactions take place in the dienol series.

The unrearranged acetate (III; R = OAc) is hydrolysed by refluxing with methyl-alcoholic potassium

* Patent application pending.

† The failure of the acetate (III; R = OAc) to isomerise on heating in benzonitrile is difficult to reconcile with its behaviour in acetic anhydride and with the experience of Burton (J., 1928, 1650), who observed the ready rearrangement of α-phenylallyl *p*-nitrobenzoate on heating in either benzonitrile or acetic anhydride, the similar behaviour in the two solvents being attributed to their similarly high dielectric constants and ionising powers.

carbonate, but with methyl alcohol alone some of the rearranged methyl ether (IV; R = OMe) is formed. Such etherifications have been effected with acetates of acetylenylcarbinols (cf. Moureu, Dufraisse, and Houghton, *Bull. Soc. chim.*, 1927, **41**, 53), and the isomerisation observed here must be brought about by the acetic acid originally liberated.

Condensation between the rearranged acetate (IV; R = OAc) and maleic anhydride in benzene gives the *anhydride* of the acid (V; R = OAc), which is converted into the *acid* on refluxing with water. On the other hand, when the addition reaction is effected in alcoholic solution a *monoethyl* ester of the acid (V; R = OAc) results. Hydrolysis of either the acetate-anhydride or the acetate-acid by heating for a few minutes with concentrated hydrochloric acid gives a lactonic *acid*, m. p. 176·5° (VI), rather unexpectedly different from that (m. p. 157—158°) obtained directly from the corresponding carbinol (Part XIX). Its *monomethyl* ester has practically the same m. p. as that of the isomeric compound, but the *mono*-p-*toluidide* is readily distinguishable from the corresponding derivative of the other form. Mixtures of the acids, the esters, or the toluidides melt at temperatures intermediate between the m. p.'s of the two components.

These two forms of (VI) are almost certainly stereoisomerides, and it seems likely that the treatment with boiling hydrochloric acid permits the assumption of the more stable configuration before lactonisation. The possibility of interconversions between the two forms and their inter-relationship will be examined as occasion permits.

A further indication of the great mobility of the system present in propenylvinylcarbinol is provided when, in attempts to prepare its hydrogen phthalate in pyridine solution at room temperature, the *hydrogen phthalate* of the rearranged alcohol (IV; R = OH), exhibiting intense light absorption in the ultra-violet (Table), is produced.

On the other hand, the lower mobility of divinylcarbinol (VII; R = OH) is clearly demonstrated in that with methyl-alcoholic sulphuric acid only the *methyl ether* (VII; R = OMe) of the unrearranged carbinol is produced, and refluxing with acetic anhydride gives only the unrearranged *acetate* (VII; R = OAc). The structures of both compounds follow from their inability to absorb in the ultra-violet and their failure to react with maleic anhydride. This stability of divinylcarbinyl acetate (VII; R = OAc) in boiling acetic anhydride is unexpected in view of the ready isomerisation of the parent carbinol (VII; R = OH), and this result would appear to be contrary to the postulates of Burton and Ingold (J., 1928, 904) that the mobility of the anion X increases in the order X = OH < OAc < Cl < Br, *i.e.*, in the order of increasing ionic stability. However, the basis on which true comparisons could be made is not obvious and, if the prediction is intended to apply to spontaneous rearrangements, *i.e.*, in the absence of acids, as well it might, it is probably true.

$CH_2{:}CH{\cdot}CHR{\cdot}CH{:}CH_2$
(VII.)

Experimental.

(Absorption spectra were determined in alcoholic solutions.)

2-Ethoxyhexa-3 : 5-diene (IV; R = OEt).—Propenylvinylcarbinol (116 g.; preceding paper) was added slowly to a cold solution of concentrated sulphuric acid (4 g.) in alcohol (400 c.c.), the mixture set aside at room temperature for 20 hours, then diluted with water, and the product isolated with ether. Removal of the latter through a column, and distillation of the product through a 24-cm. Dufton column, gave *2-ethoxyhexa-3 : 5-diene* (85 g.) as a mobile liquid with a pronounced ethereal odour; b. p. 62—62·5°/77 mm., $n_D^{17°}$ 1·4484 (Found: C, 75·9; H, 11·05. $C_8H_{14}O$ requires C, 76·15; H, 11·2%).

2-Methoxyhexa-3 : 5-diene (IV; R = OMe).—Prepared by the above method from propenylvinylcarbinol (30 g.), methyl alcohol (100 c.c.), and sulphuric acid (1 g.), the *ether* (18 g.) had b. p. 61—62°/100 mm., $n_D^{19°}$ 1·4488 (Found: C, 74·75; H, 10·9. $C_7H_{12}O$ requires C, 74·95; H, 10·8%).

2-β-Chloroethoxyhexa-3 : 5-diene (IV; R = $CH_2Cl{\cdot}CH_2O$).—A mixture of propenylvinylcarbinol (30 g.), ethylene chlorohydrin (100 c.c.), and sulphuric acid (1 g.) was kept at room temperature for 2½ days. Isolation in the usual manner, followed by careful fractionation, gave the *β-chloroethyl ether* (9 g.), b. p. 79·5°/7·5 mm., $n_D^{22·5°}$ 1·4910 (Found: C, 59·8; H, 8·0. $C_8H_{13}OCl$ requires C, 59·85; H, 8·15%).

3-α-Ethoxyethyl-Δ⁴-cyclohexene-1 : 2-dicarboxylic Acid (V; R = OEt).—Equimolecular quantities of the above ethyl ether and maleic anhydride were brought to reaction in benzene solution. The crystals which separated on evaporation were recrystallised several times from light petroleum (b. p. 40—60°), giving the *anhydride* as needles, m. p. 68° (Found: C, 64·35; H, 7·3. $C_{12}H_{16}O_4$ requires C, 64·25; H, 7·2%). Refluxing with water gave the *acid*, which formed hexagonal plates, m. p. 165·5—166° (Found: C, 59·55; H, 7·5. $C_{12}H_{18}O_5$ requires C, 59·5; H, 7·5%).

3-α-Methoxyethyl-Δ⁴-cyclohexene-1 : 2-dicarboxylic Acid (V; R = OMe).—The *anhydride*, prepared as above, formed prismatic needles, from light petroleum (b. p. 80—100°), m. p. 85—86° (Found: C, 62·9; H, 6·55. $C_{11}H_{14}O_4$ requires C, 62·85; H, 6·7%). Refluxing with water gave the *acid* as rectangular prisms, m. p. 163—164° (Found: C, 57·9; H, 6·85. $C_{11}H_{16}O_5$ requires C, 57·9; H, 7·05%).

3-Acetoxyhexa-1 : 4-diene (III; R = OAc).—Acetic anhydride (68 g.) was gradually added to a cooled solution of propenylvinylcarbinol (65 g.) in pyridine (60 g.), and the mixture kept for 5 days at about 20°. After shaking with water for 30 mins., isolation with ether gave *3-acetoxyhexa-1 : 4-diene* (85·5 g.), b. p. 60°/20 mm., $n_D^{19°}$ 1·4384 (Found: C, 68·75; H, 8·75. $C_8H_{12}O_2$ requires C, 68·55; H, 8·65%). *Light absorption:* Doubtful max. 2230 A.; ε = 1,500.

When this acetate (10 g.) was heated under reflux for 6 hours in methyl alcohol (10 c.c.) in the presence of anhydrous potassium carbonate (5 g.), there was obtained propenylvinylcarbinol (6·7 g.), b. p. 96—98°/150 mm., $n_D^{18°}$ 1·4542. The α-naphthylurethane had m. p. 94—95°, undepressed on admixture with an authentic specimen (Part XIX).

Refluxing the acetate (10 g.) in methyl alcohol (15 c.c.) for 7 hours gave a heterogeneous product from which on fractionation 2-methoxyhexa-3 : 5-diene (2·2 g.), b. p. 77—78°/150 mm., $n_D^{18°}$ 1·4508, was obtained. *Light absorption:* Maximum, 2230 A., ε = 24,000. With maleic anhydride in benzene it gave the adduct, m. p. 84—85°, undepressed on admixture with an authentic specimen (see above).

2-Acetoxyhexa-3 : 5-diene (IV; R = OAc).—(*a*) A solution of hexa-3 : 5-dien-2-ol (65 g.; Heilbron, Jones, McCombie, and Weedon, preceding paper) in pyridine (60 g.) was treated with acetic anhydride (68 g.), and the mixture kept at

about 20° for 2 days. This yielded *2-acetoxyhexa-3 : 5-diene* (77 g.), b. p. 66—70°/20 mm., $n_D^{20.5°}$ 1·4579 (Found: C, 68·25; H, 8·5. $C_8H_{12}O_2$ requires C, 68·55; H, 8·65%).

(*b*) When hexa-3 : 5-dien-2-ol (10 g.) was heated with acetic anhydride (12 g.) on a steam-bath for 5 hours in an atmosphere of nitrogen, 2-acetoxyhexa-3 : 5-diene (9·5 g.), b. p. 68—70°/20 mm., $n_D^{17°}$ 1·4597, was obtained.

(*c*) A solution of propenylvinylcarbinol (100 g.) in acetic anhydride (120 g.) was heated for 3 hours on a steam-bath in an atmosphere of nitrogen, giving 2-acetoxyhexa-3 : 5-diene (60 g.), b. p. 63—66°/20 mm., $n_D^{18°}$ 1·4583.

(*d*) A solution of 3-acetoxyhexa-1 : 4-diene (10·7 g.) in acetic anhydride (15 c.c.) was heated on a steam-bath for 40 hours. Isolation in the usual manner gave 2-acetoxyhexa-3 : 5-diene (5·5 g.), b. p. 58·5—60·5°/13 mm., $n_D^{15°}$ 1·4632. This material was slightly contaminated with an impurity of higher refractive index, but it gave the expected maleic anhydride adduct (see below), m. p. 142—143°, undepressed on admixture with an authentic specimen.

3-α-Acetoxyethyl-Δ⁴-cyclohexene-1 : 2-dicarboxylic Acid (V; R = OAc).—A mixture of 2-acetoxyhexa-3 : 5-diene (10 g.) and maleic anhydride (7·5 g.) was dissolved in benzene (25 g.) and after the solution had stood for 3 days at about 20° a mass of needles separated. These, together with a further quantity obtained on concentrating the benzene solution, when recrystallised from methyl alcohol gave the *anhydride* (8·4 g.) of the above acid, as needles, m. p. 142—143° (Found: C, 60·7; H, 6·0. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%). The *acid* crystallised from water in plates, m. p. 152·5—154° (Found: C, 56·4; H, 6·65. $C_{12}H_{16}O_6$ requires C, 56·25; H, 6·3%). The *dimethyl* ester, prepared with diazomethane, separated from aqueous methyl alcohol in needles, m. p. 103—103·5° (Found: C, 59·05; H, 7·35. $C_{14}H_{20}O_6$ requires C, 59·15; H, 7·1%). *Monoethyl ester.* Equimolecular quantities of the acetate and maleic anhydride were dissolved in alcohol. The crystalline deposit which soon separated redissolved on standing for 3 weeks at about 20°, and evaporation of the solution and crystallisation of the residue from water gave the *monoethyl* ester as needles, m. p. 120—121° (Found: C, 59·15; H, 7·25. $C_{14}H_{20}O_6$ requires C, 59·15; H, 7·1%).

γ-Lactone of 3-α-Hydroxyethyl-Δ⁴-cyclohexene-1 : 2-dicarboxylic Acid (VI).—When either the anhydride or the acid described above was refluxed with concentrated hydrochloric acid for 5 minutes the lactonic *acid* was formed. It was purified by sublimation at 100° (bath temp.)/10^{-4} mm. and by recrystallisation from water and formed plates, m. p. 176·5° [Found: C, 61·35; H, 6·2; *M* (titration), 194·5. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·15%; *M*, 196]. The *methyl* ester had m. p. 140·5—141° (Found: C, 62·9; H, 7·0. $C_{11}H_{14}O_4$ requires C, 62·85; H, 6·7%). The *p-toluidide* crystallised from aqueous alcohol as needles, m. p. 185—186° (Found: C, 71·55; H, 6·7. $C_{17}H_{19}O_3N$ requires C, 71·55; H, 6·7%).

Hydrogen Phthalate of Hexa-3 : 5-dien-2-ol.—Phthalic anhydride (15 g.) was added to a solution of propenylvinylcarbinol (10 g.) in pyridine (10 c.c.), the mixture kept at about 20° until homogeneous (5 days), and diluted with ether; the ethereal solution was washed with water, dilute hydrochloric acid, and dilute ammonium hydroxide. The alkaline washings were extracted with ether and acidified with dilute hydrochloric acid; the product (11 g.), isolated with chloroform, was an oil which gradually solidified when kept in a vacuum desiccator. Repeated crystallisation from light petroleum (b. p. 40—60°) gave the *hydrogen phthalate* of *hexa-3 : 5-dien-2-ol* as crystals, m. p. 78—80° (Found: C, 68·15; H, 6·05. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·75%).

3-Methoxypenta-1 : 4-diene (VII; R = OMe).—A mixture of divinylcarbinol (5 g.; preceding paper), methyl alcohol (10 c.c.), and concentrated sulphuric acid (0·1 g.) was kept at about 20° for one week. Isolation by means of ether gave *3-methoxypenta-1 : 4-diene* (2·7 g.), b. p. 80—82°/200 mm., $n_D^{17·5°}$ 1·4397 (Found: C, 73·5; H, 10·65. $C_6H_{10}O$ requires C, 73·4; H, 10·25%).

3-Acetoxypenta-1 : 4-diene (VII; R = OAc).—Divinylcarbinol (5·3 g.) was heated under reflux for 4 hours with acetic anhydride (10·8 g.) in the presence of anhydrous potassium acetate (1 g.). Isolation by means of ether gave *3-acetoxypenta-1 : 4-diene* (6 g.), b. p. 132°/750 mm., 74—75°/100 mm., $n_D^{16°}$ 1·4247 (Found: C, 66·85; H, 8·2. $C_7H_{10}O_2$ requires C, 66·65; H, 8·0%).

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24. *Studies in the Polyene Series. Part XXI. Ethynylcarbinols from αβ-Unsaturated Ketones: their Anionotropic Rearrangements and other Reactions.*

By J. CYMERMAN, I. M. HEILBRON, and E. R. H. JONES.

A careful study of the reaction conditions reveals that by using several mols. of sodium acetylide, made from sodamide in liquid ammonia solution, ethynylcarbinols from methyl vinyl ketone, ethylideneacetone, and mesityl oxide can be prepared in 40—55% yields. The carbinols all undergo anionotropic rearrangements on treatment with acids, although that derived from methyl vinyl ketone required the use of 10% sulphuric acid, a behaviour not unexpected, however, in view of the inability of vinylethynylcarbinol to rearrange with 25% acid. The structures of the isomerisation products are indicated by their absorption spectra and rigidly proved by complete hydrogenation to known saturated carbinols. The ethynylcarbinol from ethylideneacetone has been partly hydrogenated to the vinylcarbinol which rearranges to the secondary, rather than to the primary, dienol.

The procedure outlined above fails to give a reasonable yield of the ethynylcarbinol from *iso*phorone. Hexynylmagnesium bromide, however, yields the tertiary carbinol (XIV), which is exceptionally sensitive to acids. With 0·01% sulphuric acid the isomeric tertiary carbinol (XV) is formed, but the use of stronger acids leads to dehydration.

Both active hydrogen atoms in conjugated ethynylvinylcarbinols (*e.g.*, II), unlike those of their unconjugated isomers, react completely in the cold with methylmagnesium iodide in Zerewitinoff determinations (cf. Part VI).

ONLY two examples of the condensation of αβ-unsaturated ketones with acetylene can be found in the literature, and in both cases comparatively complex ketones were employed. The ethynylcarbinol from β-ionone was prepared by Gould and Thompson (*J. Amer. Chem. Soc.*, 1935, **57**, 340), using potassium *tert.*-amyloxide as condensing agent, and by Davies, Heilbron, Jones, and Lowe (J., 1935, 586), using sodamide. Clemo and Hoggarth (J., 1941, 476) condensed 5-keto-6 : 9-rubanene with acetylene, employing potassium *tert.*-amyloxide. With simple ketones, such as methyl vinyl ketone, which easily polymerise, the use of reagents of the above type is impracticable. It has already been shown, however (Jones and McCombie, J., 1942, 733), that condensations between αβ-unsaturated aldehydes and sodium acetylide can be carried out in liquid ammonia solution, and therefore the application of the method to αβ-unsaturated ketones has been studied in detail.

When equimolecular quantities of αβ-unsaturated ketones and sodium acetylide are mixed in liquid ammonia

solutions, the ethynylcarbinols are formed only in low yields of the order of 15%. Numerous attempts were made to vary the time of reaction and also the temperature; some experiments carried out at room temperature under pressure, and also experiments employing an excess of the ketone, met with little success. The first promising indications were obtained when an excess of sodium acetylide was employed, and with the more reactive form of the latter reagent, prepared from sodamide instead of from sodium, in liquid ammonia solution (as described in Part XVIII) reasonable yields of the desired carbinols were obtained.

By this means, 4·5 mols. of sodium acetylide being employed, methyl vinyl ketone is converted in 40% yield into the tertiary *carbinol* (I; $R_1 = R_2 = H$), which gives an *α-naphthylurethane* on long standing, and, like the other carbinols of type (I) described below, contains two active hydrogen atoms and fails to show any absorption of appreciable intensity in the ultra-violet. With 6 mols. of sodium acetylide, ethylideneacetone

(I.) $CR_1R_2{:}CH{\cdot}CMe(OH){\cdot}C{\vdots}CH \xrightarrow{acid} CR_1R_2(OH){\cdot}CH{:}CMe{\cdot}C{\vdots}CH$ (II.)

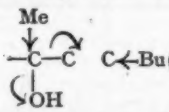
gives *3-methylhex-4-en-1-yn-3-ol* (I; $R_1 = H$, $R_2 = Me$) in 40% yield, and from mesityl oxide on treatment with 3 mols. of sodium acetylide a 55% yield of 3 : 5-*dimethylhex-4-en-1-yn-3-ol* (I; $R_1 = R_2 = Me$) (*α-naphthylurethane*) can be obtained.* The structure of the latter carbinol was proved by hydrogenation to 3 : 5-dimethylhexan-3-ol (*phenylurethane*) which was compared with a specimen made by reaction between ethylmagnesium bromide and methyl *iso*butyl ketone.

The facile rearrangement of the acetylenylcarbinols derived from αβ-unsaturated aldehydes, first described by Jones and McCombie (Part VIII; J., 1943, 261), has been considerably extended (Parts IX—XX). In Part XVI (Cymerman, Heilbron, and Jones, J., 1944, 144) the conversion of carbinols (*e.g.*, III), prepared by condensation of hexynylmagnesium bromide and αβ-unsaturated ketones, into the conjugated acetylenylvinylcarbinols (*e.g.*, IV) was reported, and it was pointed out that the rearrangements were more facile than

(III.) $CH_3{\cdot}[CH_2]_3{\cdot}C{\vdots}C{\cdot}C(OH)Me{\cdot}CH{:}CH_2 \xrightarrow{acid} CH_3{\cdot}[CH_2]_3{\cdot}C{\vdots}C{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH$ (IV.)

those of closely related secondary carbinols. It was suggested that the increased mobility of the anionotropic system was occasioned mainly by the inductive effect of the methyl group and a similar effect would be expected with the carbinols (I) described above.

It has already been reported (Jones and McCombie, *loc. cit.*) that vinylethynylcarbinol (V) fails to isomerise on treatment with 25% sulphuric acid. Its homologue (I; $R_1 = R_2 = H$), containing a tertiary hydroxyl group, is completely rearranged to (II; $R_1 = R_2 = H$) by shaking with 10% sulphuric acid for 42 hours, but with 5% acid for 18 hours isomerisation only occurs to the extent of about 25%, and with 1% acid for 24 hours the carbinol is unaffected. The marked effect of the additional methyl group is thus again apparent. On the other hand, the system present in the hexynylcarbinol (III) is clearly much more mobile than that in the

(V.) $CH_2{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH$ (VI.) 

ethynylcarbinol (I; $R_1 = R_2 = H$), since (III) is quantitatively isomerised by shaking with 0·5% sulphuric acid for 4 hours. This fact draws attention to the significance of the *n*-butyl group which, owing to its electron-repelling tendency, decreases the electron-attracting properties of the acetylenic bond, as indicated diagrammatically in (VI). A similar effect can also be produced by semihydrogenation of the triple bond (Part XIX), resulting in a greater ease of rearrangement in the case of propenylvinylcarbinol (VII) as compared with propenylethynylcarbinol (VIII).

(VII.) $CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}CH{:}CH_2$ $CH_3{\cdot}CH{:}CH{\cdot}CH(OH){\cdot}C{\vdots}CH$ (VIII.)

The rearranged *carbinol* (II; $R_1 = R_2 = H$) contains two active hydrogen atoms (Zerewitinoff) and, as would be expected of a primary alcohol, it rapidly forms an *α-naphthylurethane*. Its light-absorption properties (Table) are characteristic of those of the conjugated vinylacetylene chromophore, and its structure is finally proved by

	$\lambda_{max.}$ A.	$\varepsilon_{max.}$
3-Methylpent-2-en-4-yn-1-ol (II; $R_1 = R_2 = H$)	2235	13,000
	2280	11,500
4-Methylhex-3-en-5-yn-2-ol (II; $R_1 = H$, $R_2 = Me$)	2230	13,000
	*2340	11,500
2 : 4-Dimethylhex-3-en-5-yn-2-ol (II; $R_1 = R_2 = Me$)	2240	12,500
	*2280	11,500
Hex-3-en-5-yn-2-ol [1]	2230	13,500
	*2300	9,500

* Inflexions. [1] Jones and McCombie (*loc. cit.*).

complete hydrogenation to 3-methylpentan-1-ol. When the carbinol (I; $R_1 = H$; $R_2 = Me$) is isomerised with 1% sulphuric acid it yields *4-methylhex-3-en-5-yn-2-ol* (II; $R_1 = H$, $R_2 = Me$), characterised as its

* Since this paper was written, Hennion and Lieb (*J. Amer. Chem. Soc.*, 1944, **66**, 1289) have described condensations of sodium acetylide in liquid ammonia with methyl vinyl ketone, ethylideneacetone, and mesityl oxide. Although the constants of the ethynylcarbinols so prepared are in complete agreement with those recorded in this paper, the yields quoted range from 21 to 27%.

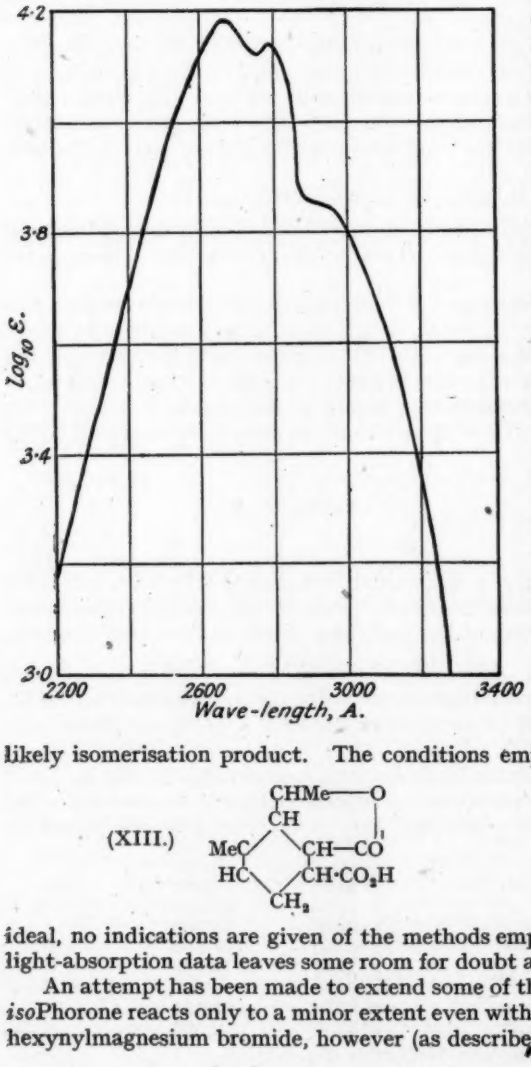
phenylurethane, giving the expected light absorption (Table) and active hydrogen values, and hydrogenated to 4-methylhexan-2-ol (3 : 5-*dinitrobenzoate*). The carbinol (I; $R_1 = R_2 = Me$) from mesityl oxide, when shaken with 0·5% sulphuric acid gives 2 : 4-*dimethylhex*-3-*en*-5-*yn*-2-*ol* (II; $R_1 = R_2 = Me$) (for light absorption, see Table).

As would be expected from the results described in Part XIX, partial hydrogenation of the acetylenic linkage in (I; $R_1 = H$, $R_2 = Me$) proceeds smoothly with a 0·3% palladium–calcium carbonate catalyst yielding 3-*methylhexa*-1 : 4-*dien*-3-*ol* (IX). It has already been shown (Part XIX) that these vinylcarbinols isomerise readily to the conjugated dienols, and in the case of (IX) two possibilities, (X) and (XI), are evident. Treatment of (IX) with 0·5% sulphuric acid gives a 50% yield of a homogeneous dienol which must be 4-*methylhexa*-3 : 5-*dien*-2-*ol* (X), since by complete hydrogenation it is converted into 4-methylhexan-2-ol. The dienol

(IX.) $CH_3{\cdot}CH{:}CH{\cdot}CMe(OH){\cdot}CH{:}CH_2$ $\qquad$ $CH_3{\cdot}CH{:}CH{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}OH$ (XI.)

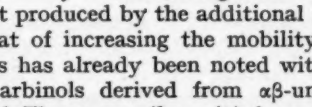
(X.) $CH_3{\cdot}CH(OH){\cdot}CH{:}CMe{\cdot}CH{:}CH_2$ $\qquad$ $OH{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CH{:}CH_2$ (XII.)

exhibits high-intensity absorption at 2290 A. ($\varepsilon = 24{,}000$) and, according to the generalisations of Woodward (*J. Amer. Chem. Soc.*, 1942, **64**, 72) concerning the effect of substituents on the location of the absorption maxima of conjugated diene systems, the maximum at 2290 A. is closer to that which would be expected for (X) ($\lambda_{max.}$ 2270 A.) than for (XI) ($\lambda_{max.}$ 2320 A.). The location is practically identical with that observed in Part XIX for a dienol (XII) structurally similar to (X). On reacting with maleic anhydride, (X) behaves in the manner characteristic (Part XIX) of conjugated dienols and yields the lactonic *acid* (XIII).



The nature of the rearrangement product in this case is that expected by analogy with the behaviour of propenylvinylcarbinol (VII) towards acids, the secondary rather than the primary carbinol being obtained (Part XIX). The only effect produced by the additional methyl group (* in IX) is that of increasing the mobility of the tautomeric system, as has already been noted with the ethynyl- and hexynyl-carbinols derived from αβ-unsaturated ketones. Gould and Thompson (*loc. cit.*) have described the conversion of the vinylcarbinol (XIV) derived from β-ionone into the primary bromide, by treatment with phosphorus tribromide and pyridine. From the results described in this and preceding papers in this series, although it would be expected that the above vinylcarbinol would be very easily isomerised, the formation of the *primary* bromo-compound appears improbable. It is conceivable, however, that factors as yet unpredictable, especially steric influences due to the presence of the unsaturated ring system, may be involved. The failure of Thompson, Milas, and Rovno (*J. Amer. Chem. Soc.*, 1941, **63**, 752) to effect rearrangement of a carbinol which they formulate as (XV) is surprising, but the desired primary carbinol seems to us to be the less likely isomerisation product. The conditions employed for the attempted isomerisations were perhaps not

(XIII.)

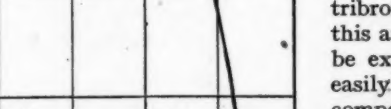


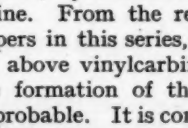
(XIV.)

ideal, no indications are given of the methods employed for detecting the expected product, and the absence of light-absorption data leaves some room for doubt as to the structure of the parent carbinol.

An attempt has been made to extend some of the observations made above to cyclic αβ-unsaturated ketones. *iso*Phorone reacts only to a minor extent even with a large excess of sodium acetylide in liquid ammonia. With hexynylmagnesium bromide, however (as described in Part XVI), it reacts readily and, after allowance for re-

(XV.)

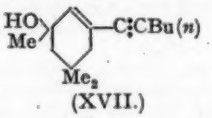


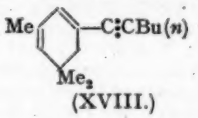


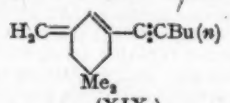
(XVI.)

covered ketone, is converted into the tertiary *carbinol* (XVI) in 85% yield. This carbinol is very sensitive towards acids, and in the presence of 0·01% sulphuric acid it undergoes rearrangement to the carbinol (XVII)

which absorbs at 2280 A. (ε = 13,500), as might be expected. With more concentrated acids, rearrangement is followed by complete dehydration; *e.g.*, with 0·5% sulphuric acid a *hydrocarbon* is obtained which, on account


(XVII.)


(XVIII.)


(XIX.)

of its light-absorption properties (Fig.), is considered to consist of a mixture of (XVIII) and (XIX), predominantly the latter. The maxima at 2660 and 2780 A. can be attributed to the form (XIX) containing the exocyclic methylene group, and the inflexion at 2915 A. to (XVIII) containing the fully cyclic diene chromophore, which by itself would be expected to absorb in the region of 2650 A. (cf. Booker, Evans, and Gillam, J., 1940, 1453). Ozonolysis of the hydrocarbon mixture gave formaldehyde, estimated as the dimedon derivative, in 50% yield, proving the presence in major proportion of (XIX).

In Part VI (J., 1942, 733) attention was directed to the behaviour of simple ethynylcarbinols during Zerewitinoff determinations of active hydrogen by means of methylmagnesium iodide, and it was noted that, whereas the hydroxyl group generally reacts completely in the cold, heating to 90° is necessary to complete the reaction with the acetylenic hydrogen atom. Many additional examples of this phenomenon have been encountered during the course of this work, but it has been observed that in the case of conjugated ethynylvinylcarbinols (such as II), replacement of the acetylenic hydrogen atom usually proceeds to completion in the cold. This implies that the hydrogen atom is more acid in character, *i.e.*, that the ≡C–H bond becomes weaker. This can be visualised as being consequent upon the contribution of electrons from the triple bond to the resonance form of the conjugated vinylacetylene system. It has previously been noted that, unlike the alkylacetylenes, vinyl- and phenyl-acetylenes form potassium derivatives even with powdered potassium hydroxide in ethereal suspension, and also that replacement halogenation of the acetylenic hydrogen atom is more facile with these conjugated compounds.

Experimental.

(Absorption spectra were determined in alcoholic solutions.)

3-Methylpent-4-en-1-yn-3-ol (I; $R_1 = R_2 = H$).—To a solution of sodium acetylide, prepared from sodium (36 g.) in liquid ammonia (1 l.) by using the ferric nitrate catalyst of Vaughn, Vogt, and Nieuwland (*J. Amer. Chem. Soc.*, 1934, **56**, 2120) to catalyse the formation of sodamide, a solution of methyl vinyl ketone (24 g.) in dry ether (250 c.c.) was added during 1½ hours with stirring and cooling (acetone–solid carbon dioxide). The mixture was stirred and cooled for a further 1½ hours; ammonium chloride (100 g.) was then added, and the ammonia allowed to evaporate off overnight. The product was isolated by means of ether, and distillation through a column with a packed section (30 × 1·5 cm.) of single-turn glass helices gave *3-methylpent-4-en-1-yn-3-ol* (12·5 g.) as a colourless pleasant-smelling liquid, b. p. 63·5—64·5°/100 mm., $n_D^{15°}$ 1·4490 (Found: C, 75·1; H, 8·45. C_6H_8O requires C, 75·0; H, 8·4%). *Active hydrogen* (Zerewitinoff): At 20°/768 mm. the carbinol (57 mg.) rapidly evolved 14·2 c.c. of methane and a further 14·6 c.c. after being heated to 90°, equivalent to 1·0 and 2·05 active hydrogen atoms per mol. respectively. Neither this carbinol, nor those from ethylideneacetone or mesityl oxide, described below, showed light absorption of appreciable intensity in the ultra-violet. The *α-naphthylurethane*, formed after 5 months' standing at 20°, crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 110—111° (Found: N, 5·45. $C_{17}H_{18}O_2N$ requires N, 5·3%).

3-Methylhex-4-en-1-yn-3-ol (I; $R_1 = H$, $R_2 = Me$).—Prepared from ethylideneacetone (42 g.) and sodium (69 g.) by the method described above, the *carbinol* (21·5 g.) had b. p. 59°/23 mm., $n_D^{19°}$ 1·4550 (Found: C, 76·45; H, 9·2. $C_7H_{10}O$ requires C, 76·3; H, 9·15%). *Active hydrogen:* At 22°/766 mm. the carbinol (55 mg.) rapidly evolved 12·7 c.c. of methane, and a further 11·6 c.c. after being heated to 90° (1·0 and 1·95 active hydrogen atoms per mol. respectively).

3 : 5-Dimethylhex-4-en-1-yn-3-ol (I; $R_1 = R_2 = Me$).—The method described above, using mesityl oxide (98 g.) and sodium (69 g.), gave the *carbinol* (68 g.), b. p. 92·5—93·5°/70 mm., 67—67·5°/22 mm., $n_D^{23°}$ 1·4619, as a colourless pleasant-smelling liquid (Found: C, 77·55; H, 10·2. $C_8H_{12}O$ requires C, 77·4; H, 9·75%). *Active hydrogen:* At 23°/770 mm. the carbinol (60 mg.) evolved 12·5 c.c. of methane and a further 11·5 c.c. on heating to 90° (1·05 and 2·05 active hydrogen atoms per mol. respectively). The *α-naphthylurethane*, obtained after keeping an equimolar mixture of the reactants in a sealed tube at 20° for 3 months, crystallised from light petroleum (b. p. 60—80°) in rhombs, m. p. 129·5—130° (decomp.) (Found: N, 4·9. $C_{19}H_{19}O_2N$ requires N, 4·8%).

3 : 5-Dimethylhexan-3-ol.—Hydrogenation of 3 : 5-dimethylhex-4-en-1-yn-3-ol (5·4 g.) in ethyl acetate (20 c.c.), using platinic oxide (100 mg.) as catalyst, gave 3 : 5-dimethylhexan-3-ol (5·2 g.), b. p. 62—63°/22 mm., $n_D^{21°}$ 1·4268. A synthetic specimen made from ethylmagnesium bromide and methyl *iso*butyl ketone had b. p. 60—60·5°/20 mm., $n_D^{21°}$ 1·4265 (Meyr and Tuot, *Compt. rend.*, 1933, **196**, 1231, give b. p. 59°/15 mm., $n_D^{20°}$ 1·4266). Identical *phenylurethanes* were obtained from either specimen of carbinol, after equimolar mixtures of carbinol and phenyl *iso*cyanate had been kept for 5 months. They separated from light petroleum (b. p. 40—60°) in needles, m. p. 62—63°, undepressed on admixture with each other (Found: N, 5·6. $C_{15}H_{23}O_2N$ requires N, 5·6%).

3-Methylpent-2-en-4-yn-1-ol (II; $R_1 = R_2 = H$).—3-Methylpent-4-en-1-yn-3-ol (4·4 g.) was shaken with sulphuric acid (80 c.c.; 10% w/v) for 42 hours at 20° in nitrogen. Ether extraction gave *3-methylpent-2-en-4-yn-1-ol* (3·5 g.), b. p. 85—87°/50 mm., 66—66·5°/30 mm., $n_D^{16°}$ 1·4850, as a colourless oil which rapidly became yellow on keeping (Found: C, 75·3; H, 8·4. C_6H_8O requires C, 75·0; H, 8·4%). *Active hydrogen:* At 20°/767 mm. the carbinol (32 mg.) rapidly evolved 7·9 c.c. of methane, and a further 7·8 c.c. after prolonged shaking (1·0 and 2·0 active hydrogen atoms per mol., respectively). The *α-naphthylurethane*, formed from the mixed reactants in 1 hour at 20°, crystallised in needles, m. p. 119°, from light petroleum (b. p. 60—80°) (Found: N, 5·3. $C_{17}H_{15}O_2N$ requires N, 5·3%).

3-Methylpentan-1-ol.—A solution of 3-methylpent-2-en-4-yn-1-ol (2 g.) in methyl acetate (20 c.c.) was shaken with hydrogen in the presence of platinic oxide (100 mg.) until absorption ceased. Removal of catalyst and solvent gave 3-methylpentan-1-ol (1·6 g.), b. p. 152—153°/763 mm., $n_D^{21°}$ 1·4200 (Olivier, *Rec. Trav. chim.*, 1936, **55**, 1027, gives b. p. 152—153°, and Levene and Rothen, *J. Biol. Chem.*, 1936, **116**, 209, give $n_D^{25°}$ 1·4178). The 3 : 5-dinitrobenzoate separated from light petroleum (b. p. 40—60°) as colourless needles, m. p. 37—38° (Sutter, *Helv. Chim. Acta*, 1938, **21**, 1266, gives m. p. 38°).

4-Methylhex-3-en-5-yn-2-ol (II; R_1 = H, R_2 = Me).—A mixture of 3-methylhex-4-en-1-yn-3-ol (7 g.) and sulphuric acid (500 c.c.; 1% w/v) was shaken for 14 hours at 20° giving *4-methylhex-3-en-5-yn-2-ol* (6·1 g.), b. p. 71·5—72°/20 mm., $n_D^{19°}$ 1·4740, as a colourless liquid rapidly turning yellow on keeping (Found: C, 76·2; H, 9·1. $C_7H_{10}O$ requires C, 76·3; H, 9·15%). *Active hydrogen:* At 23°/764 mm. the carbinol (65 mg.) rapidly gave 14·3 c.c. of methane and a further 14·7 c.c. after heating to 90° (1·0 and 2·05 active hydrogen atoms per mol., respectively). The *phenylurethane* crystallised from methyl alcohol in plates, m. p. 94—95° (Found: N, 6·3. $C_{14}H_{15}O_2N$ requires N, 6·1%).

4-Methylhexan-2-ol and *4-Methylhexan-2-one.*—A solution of 4-methylhex-3-en-5-yn-2-ol (5·5 g.) in methyl acetate (30 c.c.) was hydrogenated with platinic oxide (100 mg.) as catalyst and gave 4-methylhexan-2-ol (5·3 g.), b. p. 148—150°/767 mm., 80—82°/50 mm., $n_D^{17°}$ 1·4302 (Levene and Marker, *J. Biol. Chem.*, 1931, **91**, 761, give b. p. 146—147°/760 mm.). The 3 : 5-*dinitrobenzoate* separated from methyl alcohol in needles, m. p. 51° (Found: N, 9·05. $C_{14}H_{18}O_6N_2$ requires N, 9·05%). Oxidation of the alcohol (2·35 g.) with chromic acid in sulphuric acid gave the ketone (1·9 g.), b. p. 62—65°/50 mm., $n_D^{18°}$ 1·4118, which probably contained a little unchanged carbinol. The semicarbazone crystallised from aqueous methyl alcohol in plates, m. p. 129° (Chavanne, *Bull. Soc. chim. Belg.*, 1927, **36**, 206, gives m. p. 129°). The ketone regenerated from the pure semicarbazone by boiling with hydrochloric acid (15%) for 1 hour had b. p. 140—142°, $n_D^{20°}$ 1·4092 (Johnson and Hager, *Org. Synth.*, Coll. Vol. I, 343, give b. p. 139—142°, and Cope, Hofmann, and Hardy, *J. Amer. Chem. Soc.*, 1941, **63**, 1852, give $n_D^{25°}$ 1·4057).

2 : 4-*Dimethylhex-3-en-5-yn-2-ol* (II; R_1 = R_2 = Me).—3 : 5-Dimethylhex-4-en-1-yn-3-ol (20 g.) was isomerised by shaking with sulphuric acid (2 l.; 0·5% w/v) at 20° for 6 hours to 2 : 4-*dimethylhex-3-en-5-yn-2-ol* (15 g.), a pleasant-smelling liquid, b. p. 65—66°/20 mm., $n_D^{19°}$ 1·4711 (Found: C, 77·2; H, 9·85. $C_8H_{12}O$ requires C, 77·4; H, 9·75%). *Active hydrogen:* At 24°/769 mm. the carbinol (45 mg.) rapidly evolved 9·9 c.c. of methane and a further 8·2 c.c. on heating to 50° (equivalent to 1·1 and 2·0 active hydrogen atoms per mol. respectively).

3-Methylhexa-1 : 4-dien-3-ol (IX).—A solution of 3-methylhex-4-en-1-yn-3-ol (11 g.) in methyl acetate (30 c.c.) was shaken with hydrogen in the presence of palladium–calcium carbonate (1 g.; 0·3%) until about 2·35 l. of gas at 17°/767 mm. had been absorbed. The catalyst was filtered off and the solvent removed through a column, and distillation of the residue gave *3-methylhexa-1 : 4-dien-3-ol* (10·7 g.), b. p. 41·5—42·5°/15 mm.; 56—58°/28 mm., $n_D^{23°}$ 1·4485 (Found: C, 74·95; H, 10·85. $C_7H_{12}O$ requires C, 74·95; H, 10·8%). *Active hydrogen* (Zerewitinoff): The carbinol (49 mg.) evolved 10·6 c.c. of methane at 20°/769 mm. (1·0 active hydrogen atom per mol.), and showed no light absorption of appreciable intensity in the ultra-violet.

4-Methylhexa-3 : 5-dien-2-ol * (X) (with J. T. McCombie).—A mixture of the preceding carbinol (6 g.) and sulphuric acid (400 c.c.; 0·5% w/v) together with a trace of quinol was shaken for 25 minutes at 20° under nitrogen. Isolation with ether gave *4-methylhexa-3 : 5-dien-2-ol* (3 g.), b. p. 73—75°/14 mm., $n_D^{20°}$ 1·4878, together with much higher-b. p., resinous material (Found: C, 75·05; H, 11·15. $C_7H_{12}O$ requires C, 74·95; H, 10·8%). *Active hydrogen* (Zerewitinoff): The carbinol (35 mg.) evolved 7·5 c.c. of methane at 20°/768 mm. (1·0 active hydrogen atom per mol.).

γ-Lactone of 4-Methyl-3-α-hydroxyethyl-Δ⁴-cyclohexene-1 : 2-dicarboxylic Acid (XIII).—An equimolecular quantity of the preceding carbinol was added to maleic anhydride in dry benzene whereupon the anhydride completely dissolved and the temperature rose to 60—70°. The crystals which separated on standing and after cooling were recrystallised from benzene or water, giving the lactonic *acid* as rectangular plates, m. p. 193—194° (Found: C, 62·9; H, 7·0. $C_{11}H_{14}O_4$ requires C, 62·85; H, 6·7%).

4-Methylhexan-2-ol.—A solution of 4-methylhexa-3 : 5-dien-2-ol (4 g.) in methyl acetate (15 c.c.) was shaken with hydrogen in the presence of platinic oxide (0·1 g.) until absorption ceased. The catalyst was filtered off and the solvent removed through a column, leaving a residue of 4-methylhexan-2-ol (3·8 g.), b. p. 81—82°/50 mm., $n_D^{18°}$ 1·4298 (cf. above). The 3 : 5-dinitrobenzoate crystallised from alcohol as needles, m. p. 51°, undepressed on admixiture with an authentic specimen.

1-(1′-Hydroxy-3′ : 5′ : 5′-trimethyl-Δ²-cyclohexenyl)hex-1-yne (XVI).—To an ice-cold solution of hexynylmagnesium bromide (Cymerman, Heilbron, and Jones, *loc. cit.*), prepared from 1-hexyne (12·5 g.) and ethylmagnesium bromide (from 3 g. of magnesium), a solution of *iso*phorone (17·2 g.; b. p. 99°/21 mm., $n_D^{18°}$ 1·4785) in ether (200 c.c.) was added with stirring during 1½ hours. After a further 18 hours' stirring at 20° the Grignard complex was decomposed with ammonium chloride solution, and isolation of the product in the usual manner followed by distillation gave a forerun of *iso*phorone (10·2 g.) and the *carbinol* (10·1 g.), as a colourless viscous oil with a faint odour of eucalyptus; b. p. 107·5—108·5°/10^{-3} mm., 58° (bath temp.)/10^{-4} mm., $n_D^{21°}$ 1·4900 (Found: C, 81·7; H, 10·7. $C_{15}H_{24}O$ requires C, 81·75; H, 11·0%). *Active hydrogen* (Zerewitinoff): The carbinol (116 mg.) evolved 12·6 c.c. of methane at 20°/763 mm. (1·0 active hydrogen atom per mol.). It showed no appreciable light absorption in the ultra-violet.

1-(3′-Hydroxy-3′ : 5′ : 5′-trimethyl-Δ¹′-cyclohexenyl)hex-1-yne (XVII).—The preceding carbinol (1·2 g.) was treated with sulphuric acid (1000 c.c.; 0·01% w/v) containing acetone (300 c.c.) for 30 minutes at 20° under nitrogen. Isolation with ether afforded the rearranged *carbinol* (XVII) (1 g.), which has a faint camphoraceous odour, b. p. 54° (bath temp.)/10^{-4} mm., $n_D^{18°}$ 1·5019 (Found: C, 81·45; H, 11·4. $C_{15}H_{24}O$ requires C, 81·75; H, 11·0%). *Active hydrogen* (Zerewitinoff): The carbinol (82 mg.) evolved 8·9 c.c. of methane at 19°/769 mm. (1·0 active hydrogen atom per mol.). *Light absorption*: Maximum, 2280 A.; ε = 13,500.

Simultaneous Rearrangement and Dehydration of (XVI).—The carbinol (5 g.) was treated with sulphuric acid (600 c.c.; 0·5% w/v) containing acetone (100 c.c.) for 16 hours at 20°. Isolation in the usual manner gave a product, $n_D^{19°}$ 1·5160. *Light absorption:* Maximum, 2645 A.; ε = 11,500. Inflexion, 2780 A.; ε = 11,000. On distillation this gave a *hydrocarbon* (3·95 g.), b. p. 110—110·5°/5 mm., 42° (bath temp.)/10^{-4} mm., $n_D^{20°}$ 1·5150 (Found: C, 89·15; H, 10·9. $C_{15}H_{22}$ requires C, 89·05; H, 10·95%). *Light absorption:* Maxima, 2660 and 2780 A.; ε = 15,000 and 14,000, respectively. Inflexion, 2915 A., ε = 7,000.

Ozonolysis of Hydrocarbon.—A solution of the hydrocarbon (1 g.) in acetic acid (25 c.c.) was treated with a stream of ozonised oxygen at 20° for 2 hours, the issuing gases being passed into water. This solution and the reaction mixture were combined and steam-distilled after the addition of zinc dust (1 g.). The distillate, treated with an excess of dimedon according to Jonescu (*Bull. Soc. chim.*, 1930, **47**, 1408), gave 0·70 g. of the dimedon derivative (m. p. and mixed m. p. 188°), corresponding to a 50% yield.

Imperial College of Science and Technology, London, S.W. 7. [*Received, October 19th*, 1944.]

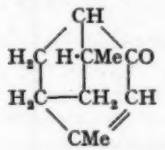
* Patent application pending.

25. *Observations on the Absorption Spectra of Terpenoid Compounds. Part V. Umbellulone.*

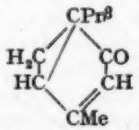
By A. E. Gillam and T. F. West.

Umbellulone and certain of its derivatives have been prepared from oil of Californian laurel such that their physical and analytical constants were identical with those of the previously described ketone. The absorption spectra of the ketone and its semicarbazone are found to be quite different from those expected of a simple $\alpha\beta$-unsaturated ketone. Since a carbonyl group in conjugation with a *cyclo*propane ring produces a measure of hyperconjugation as in carone, it is concluded that the abnormal absorption spectrum of umbellulone is due to the unusual chromophoric group consisting of a *cyclo*propane ring in crossed conjugation with a carbonyl group and an ethylene linkage.

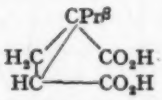
In earlier papers in this series the absorption spectra of various terpenes and related compounds have been studied with a view to obtain information that would throw light on their molecular structures (Part IV, J., 1942, 486). The subject of the present investigation—umbellulone—was first isolated from the leaves of the Californian laurel (*Umbellularia Californica*, Nuttall) by Power and Lees (J., 1904, **85**, 629) and shown to be a ketone, $C_{10}H_{14}O$. Largely on the basis of an examination of oxidation products Tutin (J., 1907, **91**, 271, 275; 1908, **93**, 252) suggested structure (I), but Semmler (*Ber.*, 1907, **40**, 5017; *loc. cit.*) preferred structure (II). Rydon's synthesis of umbellularic acid (III) (J., 1936, 829; cf. Phillips, Ramage, and Simonsen, *ibid.*, p. 828), which was shown by direct comparison to be identical with the oxidation product obtained by Tutin, was the first synthetic evidence for the presence of the *cyclo*propane ring postulated by Semmler. Later,



(I.)



(II.)



(III.)

Weinhaus and Todenhöfer (*Schimmel Berichte, Jubiläumes Ausgabe*, 1929, 285) showed that umbellulone can be separated from other constituents of laurel oil by treatment with neutral sodium sulphite and regenerated from the sulphite compound by treatment with alkali.

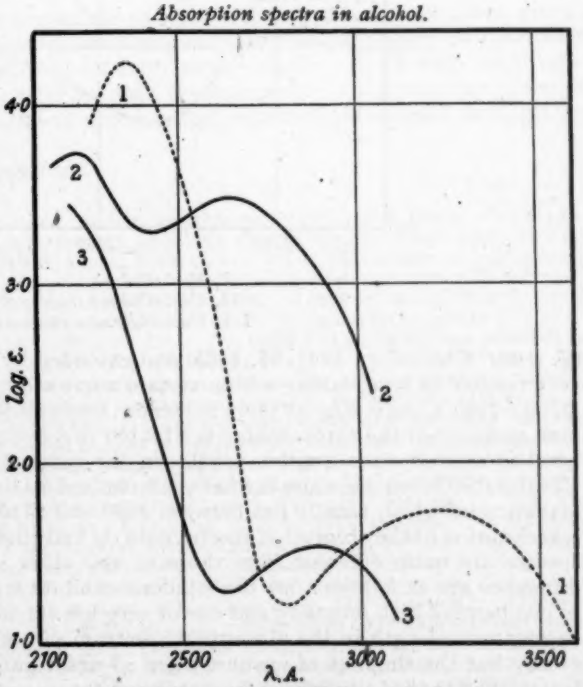
We have now subjected Californian laurel oil to fractional distillation under reduced pressure to obtain umbellulone having the appropriate constants, and then carried out the reaction with semicarbazide as described by Semmler but only obtained low yields of the semicarbazido-semicarbazone (about 50%). Small quantities of the monosemicarbazone were also obtained and (following Semmler) were separated by means of its sparing solubility in hot water.

Experiments to ascertain whether the yield of semicarbazido-semicarbazone or, better still, that of monosemicarbazone could be increased did not produce very marked improvement at first. However, it was discovered, fortuitously, that if the first crop of semicarbazones is removed together with the excess of alcohol, and the residual oil is left in contact with the aqueous reagents for some 8—10 weeks, considerably more of the monosemicarbazone is produced. By regeneration of the ketones from both the normal and the semicarbazido-semicarbazone, it has been possible to establish their identity and so confirm that the same ketone is the parent of both types of derivative.

From the foregoing it is clear that umbellulone contains a *cyclo*propane ring, an ethylene linkage, and a keto-group in a molecule $C_{10}H_{14}O$. Having obtained the absorption spectrum of the compound (Fig. 1 and Table), we sought to determine whether the >C=O and >C=C< groups are conjugated or not.

Fig. 1.

Absorption spectra in alcohol.



1, *Piperitone*. 2, *Umbellulone*. 3, *Carone*.

This is easily decided from the light-absorption data, since the isolated carbonyl group in a chromophorically simple molecule usually gives rise to an absorption band *near* 2800 A. having ε of the order of <100, whereas in an $\alpha\beta$-unsaturated carbonyl compound this band is displaced to the neighbourhood of 3000—3200 A. and a new band of much greater intensity appears between 2200 and 2500 A. (ε, order 6000—14,000). The intensity

Spectrographic Data on Umbellulone and Related Compounds.

	$\lambda_{max.}$	$\varepsilon_{max.}$		$\lambda_{max.}$	$\varepsilon_{max.}$
Umbellulone *	2200	5,000	Carone semicarbazone	2365	13,500
	2650	2,900	Piperitone thiosemicarbazone	2450	13,470
Piperitone	2355	17,780		3020	32,200
	3210	54	*Carone thiosemicarbazone*	2360	9,000
Carone	<2200	>2,680		2790	23,000
	2880	34	*Umbellulone thiosemicarbazido-thiosemicarbazone* *	2425	18,400
Umbellulone semicarbazone	2860	14,000		2785	24,600
Piperitone semicarbazone	2660	19,300	Umbellulone semicarbazido-semicarbazone	2363	16,000

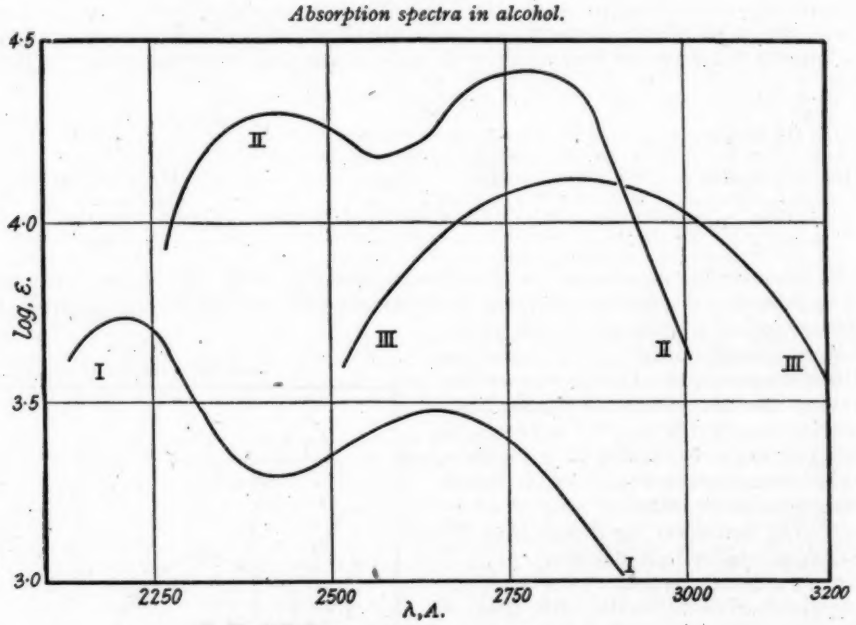
* Mean values on independent preparations.

of absorption in umbellulone is thus too high to be explained by an isolated carbonyl group and is consistent with some form of conjugated system.

From the postulated structure of umbellulone (II) we see that the most likely absorbing entity is the >C=C–C=O grouping. The light-absorption data for compounds of this type have been collected by Woodward

FIG. 2.

Absorption spectra in alcohol.

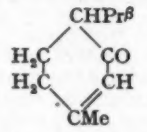


I, *Umbellulone.*
II, *Umbellulone thiosemicarbazido-thiosemicarbazone.*
III, *Umbellulone semicarbazone.*

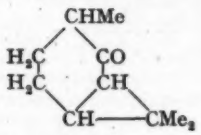
(*J. Amer. Chem. Soc.*, 1941, **63**, 1123) and extended by Evans and Gillam (J., 1941, 815) and are found to be very regular in type, falling within certain narrow limits as to location of the more intense absorption band (2200—2590 A. according as there is less or more substitution). The only disturbing factor which is relevant here arises when the chromophore is situated in a five-atom ring, for if so there is a displacement of the main band to shorter wave-lengths, usually in the range 2100—2400 A. (Gillam and West, J., 1942, 486). αβ-Unsaturated ketones are also further characterised by the light absorption of their semicarbazones, the intensity maximum of which usually lies between 2600 and 2740 A., with $\varepsilon \approx 20{,}000$ (Evans and Gillam, J., 1943, 565). Examination of the absorption spectra data on umbellulone and derivatives (Figs. and Table) shows that these spectra are quite different from those of any other αβ-unsaturated ketones yet examined. The points of difference are as follows: (*a*) Umbellulone exhibits *two* absorption bands of fairly high intensity in contrast to one band of high intensity and one of very low intensity in normal αβ-unsaturated ketones; (*b*) the band of shorter wave-length in the absorption spectrum of umbellulone is situated at a lower wave-length than that of any but the simplest of unsubstituted αβ-unsaturated ketones, and the other band lies at a longer wave-length than that of any other αβ-unsaturated ketone yet recorded; (*c*) the intensities of the umbellulone bands (order $\varepsilon = 5000$ and 3000 respectively) are unusually low for *K*-bands (usual value of ε in αβ-unsaturated ketones = 6000—14,000); (*d*) the location of the absorption band of umbellulone semicarbazone is also displaced to longer wave-lengths (λ max. = 2860 A., instead of order 2700 A.).

The nearest normal analogue of umbellulone is piperitone (IV) and the absorption spectrum of this unsaturated ketone is shown for comparison in Fig. 1.

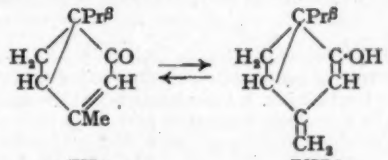
The anomalous nature of the observed absorption spectra of umbellulone and its derivatives might possibly be explained in one of three ways as follows : (*a*) the substance is a mixture of two absorbing entities or even tautomeric forms in equilibrium; (*b*) the proposed formula is not the correct one; or (*c*) the peculiar molecular environment of a *cyclo*propane ring fused to a *cyclo*pentane ring and in crossed conjugation with an ethylene linkage and a carbonyl group modifies the light absorption normally expected of an αβ-unsaturated ketone



(IV.) Piperitone.



(V.) Carone.



(VI.) (VII.)

so that it is different from anything yet encountered. The mixture hypothesis has been tested, but we have been unable to produce any signs of separation into two components either by rigorous fractional distillation or by chromatographic separation on alumina. Moreover, the umbellulone prepared by us and earlier workers has identically the same physical constants. The possibility of a tautomeric system of two components each having a different chromophoric system is difficult to support by postulation of suitable isomerides. The failure to obtain appreciable amounts of formaldehyde on ozonolysis appeared to preclude the possibility of tautomerism of the type (VI) ⇌ (VII). Furthermore it was not possible to isolate the enolic form or to prepare an enol acetate.

Although umbellulone itself has not been synthesised, the chemical evidence seems to justify the formula (II) previously put forward for the compound, so the explanation of the anomalous light-absorption data must lie in the unusual nature of the molecular structure. The only unknown quantity likely to affect the absorption spectra is the three-atom ring in conjugation with a carbonyl group and fused to a five-atom ring—a most unusual molecular environment. It has recently been shown that when a saturated three-atom ring is conjugated with a carbonyl group or an ethylene linkage a species of conjugated system is produced which affects the absorption spectrum in the sense of producing what Mulliken (*J. Chem. Physics*, 1939, **7**, 339) calls "hyperconjugation." Attention has recently been directed to this effect in carone (V) (Klotz, *J. Amer. Chem. Soc.*, 1944, **66**, 88); where the absorption spectrum approaches that of an αβ-unsaturated ketone. Our own absorption data on this compound are in the table.

If, in the accepted umbellulone formula (II), we look upon the *cyclo*propane ring as a chromophoric group, the chromophore consists of an ethylene linkage and a *cyclo*propane ring in crossed conjugation with a carbonyl group, a system for which there appears to be no suitable model substance available. Until such model substances of known structure are available, we can only conclude that the unexpected absorption spectrum of umbellulone is associated with this unusual unsymmetrical chromophoric make-up of crossed conjugation and hyperconjugation.

Experimental.

(Analyses are by Drs. Weiler and Strauss, Oxford.)

Preparation of Umbellulone Semicarbazido-semicarbazone and Monosemicarbazone.—Californian laurel oil (50 g.), having $d_{15\cdot5^\circ}^{15\cdot5^\circ}$ 0·984, α_D − 25·9°, ester value 5·8, was fractionated through an 8-bulb column to give umbellulone (19·3 g.) having b. p. 87—90°/4 mm., $d_{15\cdot5^\circ}^{15\cdot5^\circ}$ 0·950, $n_D^{20^\circ}$ 1·4832, α_D − 35·8°, λ max. 2165 A., ε = 2500. A number of experiments were carried out upon this fraction, using sodium acetate and pyridine with semicarbazide hydrochloride. In a typical experiment umbellulone (14 g.), dissolved in alcohol (70 ml.), was added to a solution of semicarbazide hydrochloride (10·75 g.) and pyridine (35 ml.) in water (10 ml.). After standing for 24 hours at the ordinary temperature and at 0° for 3 days, the crystalline deposit (8·2 g.) had m. p. 195—196° (decomp.) (A). The bulk of the alcohol was removed in a vacuum, and the product refrigerated overnight to give a second crop of crystals (1 g.), m. p. 185—220° (B). The filtrate was kept at room temperature for 2 months, a layer of red oily material occluding some crystalline material separating at the surface. Ether (20 ml.) was added, and the insoluble material removed by filtration (1·6 g., m. p. 218—223°) (C). The oil was extracted with ether, the ethereal solution washed with water, and the ether removed to give 4 g. of unchanged oil. Crops A and B (9·2 g.) were heated rapidly to boiling with water (400 ml.), and the solution filtered from insoluble material (0·6 g.) (D). Then C and D were bulked and boiled with 50 ml. of water and filtered. The filtrate was added to the 400 ml. filtrate. The water-insoluble material (1·92 g.) had m. p. 224° (indefinite, decomp.). This was recrystallised from methyl alcohol (120 ml.) to give a first crop (1·6 g.), m. p. 228—231° (decomp.). This was recrystallised from 90% w/v aqueous methyl alcohol (120 ml.) to give 1·41 g., m. p. 231—232° (decomp.). After three further recrystallisations from aqueous methyl alcohol the umbellulone semicarbazone (1·12 g.) had m. p. 238—239° (decomp.) (rapid heating, 240—242°) unchanged by further recrystallisation; λ max. 2885 A., ε 13,000 (Found : C, 63·7; H, 8·2. Calc. for $C_{11}H_{17}ON_3$: C, 63·8; H, 8·2%). The first crop from the water-soluble portion (7·7 g.) had m. p. 209° (decomp.). Recrystallised from water (300 ml.) the product (6·4 g.) had m. p. 211° (decomp.). This was recrystallised from ethyl alcohol (650 ml.) to give 6·0 g., m. p. 205—206° (decomp.), which when recrystallised from water (300 ml.) gave umbellulone semicarbazido-semicarbazone (3·9 g.), m. p. 215—216° (decomp.), λ max. 2360 A., ε 16,600 (Found : C, 50·95; H, 7·8. Calc. for $C_{12}H_{22}O_2N_6$: C, 51·1; H, 7·7%). The 4 g. of recovered unreacted oil was poured off from the small quantity of solid which was precipitated on standing and steam distilled with oxalic acid (2·5 g.), the oil being recovered from the steam distillate by ether extraction, and distilled under reduced pressure to give 2·8 g. (leaving a residue of 0·5 g.), b. p. 63—76°/2 mm., $n_D^{20^\circ}$ 1·4829, $d_{15}^{20^\circ}$ 0·9372, $[\alpha]_D$ − 26·25° (*c*, 12 in alcohol); λλ max. 2200 A., ε 3100; 2675 A., ε 1450. This recovered oil (2·6 g.) in alcohol (22 ml.) was added to a solution of semicarbazide hydrochloride (3·7 g.) in water (3·7 ml.) and pyridine (13 ml.). The mixture was kept at room temperature, then diluted with water (41 ml.) and kept at 0° for 3 weeks. The semicarbazone which separated (1·26 g.) had m. p. 193—236°. The alcohol was removed from the filtrate under reduced pressure, the residue diluted with water (250 ml.), and thoroughly extracted with ether. The ethereal solution was washed until neutral with brine, and the ether removed. The residue

was treated with water, oxalic acid (0·8 g.) added, and the oil distilled in steam. The oil (0·7 g.) recovered from the distillate by extraction with light petroleum was distilled to give 0·65 g., b. p. 56—70°/1·5 mm., $n_D^{20°}$ 1·4849, $[\alpha]_D^{20°}$ − 20·8° (in alcohol), $d_{15·5°}^{15·5°}$ 0·944, λλ max. 2200 and 2690 A., ε 1713 and 687 respectively.

Regeneration of Umbellulone.—(i) Umbellulone monosemicarbazone (1·1 g.) was steam distilled in the presence of phthalic anhydride and water (10 ml.). The umbellulone extracted from the distillate with ether and purified by distillation (0·3 g.) had b. p. 69°/3 mm., $n_D^{20°}$ 1·4846, $d_{20°}^{20°}$ 0·950, $[\alpha]_D$ − 36° (*c*, 1 in alcohol), λλ max. 2200 A., ε 4920; 2650 A., ε 2850. (ii) Umbellulone semicarbazido-semicarbazone (7·8 g.), m. p. 216—217°, was steam distilled with oxalic acid (15·6 g.) and water (30 ml.) to give by ether extraction umbellulone (3·25 g.), b. p. 72°/3 mm., $n_D^{20°}$ 1·4847, $d_{15°}^{15°}$ 0·9518, α_D − 37° (Found: C, 80·2; H, 9·8. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·3%); λλ max. 2200 A., ε 5070; 2650 A., ε 2900.

Umbellulone Thiosemicarbazido-thiosemicarbazone.—Umbellulone (0·7 g.) was added to a solution of thiosemicarbazide (0·43 g.) in 70% aqueous ethyl alcohol (14 ml.). Two drops of hydrochloric acid were added, and the solution boiled under reflux for 15 mins. After being kept at room temperature overnight and then at 0° for 24 hours, the white powdery crystals (0·19 g.) which separated had m. p. 203—204°. This product was recrystallised twice from absolute alcohol to give *umbellulone thiosemicarbazido-thiosemicarbazone* (70 mg.), m. p. 210—211° (Found: C, 46·1, 45·8; H, 7·4, 7·1. $C_{11}H_{17}N_3S$ requires C, 59·2; H, 7·6%. $C_{12}H_{22}N_6S_2$ requires C, 46·0; H, 7·0%); λλ max. 2785 A., ε 26,200; 2425 A., ε 19,800. After separation of the first crop above (m. p. 203—204°), the alcohol was removed at room temperature in a current of air until oily droplets separated at the surface. The mixture was then kept at 0° for 6 weeks, and a solid collected. This was triturated with methyl alcohol (40 ml.), and the mixture kept at 0° for 3 days. By filtration, 0·34 g. of white powdery material was obtained, m. p. 198—199°. This was twice recrystallised from *iso*propyl alcohol (50 and 40 ml.) to give 0·19 g., m. p. 209° unchanged (Found: N, 25·8. Calc. for $C_{11}H_{17}N_3S$: N, 18·8%. Calc. for $C_{12}H_{22}N_6S_2$: N, 26·75%); λλ max. 2425 A., ε 17,000; 2785 A., ε 23,000.

Ozonolysis.—This was carried out in four separate lots, the yields being bulked for working up. Umbellulone regenerated from the semicarbazido-semicarbazone (1 g.) in carbon tetrachloride (30 ml.) was subjected to a slow stream of ozonised oxygen (6 hours) and then treated with ice to decompose the ozonide (24 hours) and shaken with separate lots of water, these being finally bulked and divided into two portions, A and B, A being one-eighth of the whole sample (= 0·5 g. of umbellulone). This was extracted with water exhaustively, treated with dimedon (1·2 g.) in saturated aqueous solution, and left for 40 hours. The silky, needle-like precipitate (30·2 mg.) was filtered off and recrystallised, m. p. 190° (corr.); the pure dimedon derivative of formaldehyde had m. p. 189° (corr.), mixed m. p. 186° (corr.). The yield of formaldehyde was 0·62 g. per 100 g. of umbellulone.

Portion B, seven-eighths of the whole sample (= 3·5 g. of umbellulone), was treated as follows. The aqueous liquors were made neutral by adding N/10-sodium hydroxide (300 ml.), and the volume reduced to 100 ml. by distillation under reduced pressure. Then N/10-sulphuric acid (300 ml.) was added, and the product extracted with ether. The ether was removed, giving an oil, which was fractionated: (i) b. p. 108—110° (0·265 g.), which yielded an anilide, m. p. 101—102°, not depressed on admixture with the anilide, m. p. 103—104°, prepared directly from propionic acid; (ii) b. p. 150—220° (0·351 g.), and (iii) b. p. 220—250° (0·314 g.), were not identified. In another ozonolysis experiment the combined carbon tetrachloride and aqueous extracts were transferred to alcohol, and the absorption spectrum examined. The selective absorption was found to have disappeared and the low intensity of the general absorption indicated that the umbellulone had been effectively decomposed.

Carone and its Semicarbazone and Thiosemicarbazone.—*d*-Carone, having b. p. 95—97°/10 mm., $n_D^{20°}$ 1·4953, α_D +58·75°, $d_{15·5°}^{15·5°}$ 0·952, obtained by fractionation from English dill oil, was converted essentially as described by Klotz (*J. Amer. Chem. Soc.*, 1944, **66**, 91) into carone, having b. p. 80—82°/7 mm., $n_D^{20°}$ 1·4765, $d_{15·5°}^{15·5°}$ 0·954, $[\alpha]_D$ + 154·6°, λ max. <2200 A., ε >2680. The semicarbazone after recrystallisation from aqueous methyl alcohol had m. p. 170—172°, λ max. 2365 A., ε 13,500.

Attempts to regenerate carone were unsuccessful; for instance, the oil obtained by steam distillation in the presence of oxalic acid had b. p. 63—64°/1·5 mm., $n_D^{20°}$ 1·4785, $[\alpha]_D$ + 39·5° (*c*, 8 in alcohol), λ max. 2345 A., ε 5200. The λ max. and ε values showed that a change had occurred during regeneration resulting in the formation of an αβ-unsaturated ketone (probably monocyclic). This ketone did not yield a crystalline semicarbazone, and as the observation was irrelevant to the present work it was not further investigated.

Carone thiosemicarbazone was prepared as follows. Carone (0·4 g.) in alcohol (22 ml.) was added with stirring to a cold solution of thiosemicarbazide (0·28 g.) in water (14 ml.), to which one drop of 10% hydrochloric acid had been added. After standing for 20 hours at room temperature, the mixture was refrigerated for 12 hours. Then water was added slowly until no further crystalline material separated. The white, waxy crystals (0·13 g.) had m. p. 125° (sintering at 118°), raised by one recrystallisation from aqueous (70%) methyl alcohol (5 ml.) to 131—132° (Found: N, 19·7. $C_{11}H_{19}N_3S$ requires N, 18·7%); λλ max. 2360 A., ε 9000; 2790 A., ε 23,000.

Determinations of absorption spectra were made in ethyl-alcoholic solution on a Hilger E_3 quartz spectrograph in conjunction with a Spekker photometer.

One of us (T. F. W.) is indebted to the Directors of Messrs. Stafford Allen and Sons Ltd. for facilities.

THE UNIVERSITY, MANCHESTER.
STAFFORD ALLEN AND SONS, LTD., LONDON, N. 1.

[*Received, October 25th*, 1944.]

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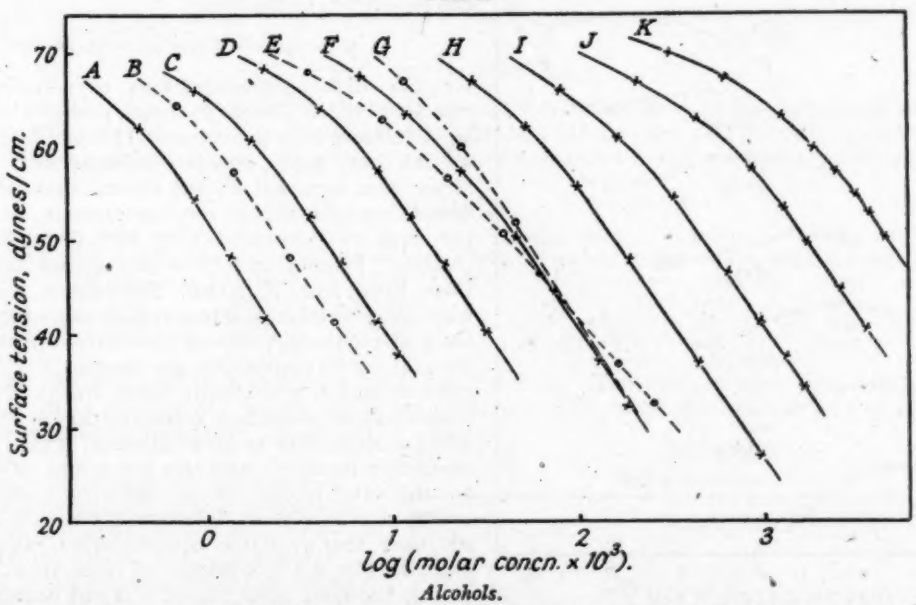
26. *The Properties of Freshly Formed Surfaces. Part IV. The Influence of Chain Length and Structure on the Static and the Dynamic Surface Tensions of Aqueous-alcoholic Solutions.*

By C. C. ADDISON.

The vibrating-jet technique already described has been applied to the measurement of both static and dynamic surface tensions of aqueous solutions of alcohols containing from one to eight carbon atoms. The static tensions at high concentration have been used to evaluate the Szyszkowski constants, and the work of adsorption has been deduced from the static tensions at great dilution. Dynamic surface tensions are recorded for aqueous solutions of *n*-amyl, *n*-hexyl, *n*-heptyl, and *n*-octyl alcohols over a range of surface ages, and the migrational velocity has been shown to increase with increasing chain length. Branching of the carbon chain (as in *iso*amyl or *tert.*-hexyl alcohol) or alteration in the position of the hydroxyl group (as in *sec.*-octyl alcohol) appears to reduce the migrational velocity, and possible reasons for this are discussed.

THE mean velocity of migration of *sec.*-octyl alcohol molecules to the air–water surface reported in Part III (J., 1944, 477) is appreciably greater than that for *iso*amyl alcohol (Part II, *ibid.*, p. 252). Since the structure of the carbon chain differs in the two cases, the values cannot be taken as more than an indication of the influence of increasing chain length. The investigation has now been extended to the measurement of the rate at which equilibrium is established for a range of alcohols in aqueous solution, and the chain-length effect has been accurately determined. The influence of structure on migrational velocity is not yet clear, but the available evidence is now reviewed. Solubility considerations limited the present study to the 1—8 carbon atom range, and although static surface tensions are fairly well established for aqueous solutions of the lower members, fewer previous measurements have been made on the higher members. In some cases the relevant constants have not previously been determined, and the concentration ranges are limited. Preliminary work with the *n*-alcohols indicated that chain length was one of the major factors determining migrational velocity, and that the presence in the alcohol samples of small amounts of impurity of longer chain length seriously impaired the accuracy of measurement. The presence of such impurity is reflected in the static curves also, and the dynamic systems were not studied until it had been confirmed that the static tensions given by the actual alcohols to be used obeyed Traube's rule. Over most of the concentration and chain-length ranges studied, the change in wave-length set up in a vibrating jet by adsorption processes ceased before the end of the jet, and the wave-length reached a steady value corresponding to the equilibrium surface.

FIG. 1.



Alcohols.

A, n-*Octyl*. B, sec.-*Octyl*. C, n-*Heptyl*. D, n-*Hexyl*. E, tert.-*Hexyl* (1 : 1-*dimethylbutyl*). F, n-*Amyl*. G, iso*Amyl*. H, n-*Butyl*. I, n-*Propyl*. J, *Ethyl*. K, *Methyl*.

The technique already described (J., 1943, 535; *Phil. Mag.*, in the press) has been thus applied to the study of both static and dynamic tensions. The static values comply closely with the rules governing an homologous series, and the dynamic tensions obtained have therefore been accepted as a reliable basis on which to assess the influence of chain length and structure.

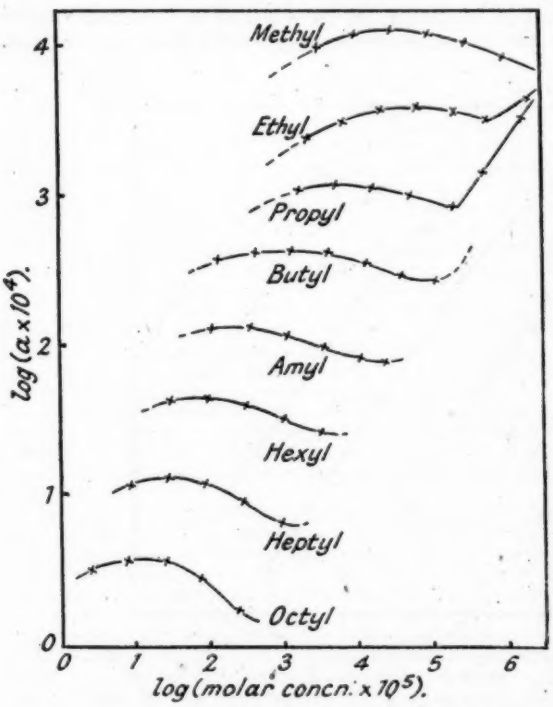
Static Surface Tensions.—The relation between equilibrium surface tension at 20°, and molar concentration for the *n*-alcohols from methyl to octyl is shown in Fig. 1. The tension values have been calculated from the wave-length by using the mathematical technique given in Part I (J., 1943, 535). The results have been checked by the drop-weight method, and in all cases agreement was within experimental error. With the most dilute solutions of the higher alcohols, the time required for establishment of equilibrium was greater than that available in the jet, and this section of the curve was determined by the drop-weight method alone. There was no detectable break where the method of measurement changed. A full review of the static surface-tension measurements which have been made by previous workers on aqueous alcohol solutions is outside the purpose and scope of the present paper. The values available are in many cases on isolated alcohols of unknown purity, but where concentration ranges overlap, the results in Fig. 1 are in good agreement with the most reliable of these (*e.g.*, Traube, *Annalen*, 1891, **265**, 27; Pederson, *Phil. Trans.*, 1907, *A*, **207**, 341; Bond and Puls, *Phil. Mag.*, 1937, **24**, 864). The agreement between values obtained by static methods such as drop weight and capillary rise, and the equilibrium values obtained from the vibrating jet, makes it clear that the condition of surface equilibrium holding when the surface is several minutes old is that which is established immediately adsorption is complete.

Below a tension of about 55 dynes/cm., the surface tension γ is a linear function of the logarithm of the concentration C for each *n*-alcohol, and this part of the curve is represented by the relation

$$\gamma = \alpha - \beta \log C \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

(where α and β are constants) proposed by Milner (*Phil. Mag.*, 1907, **23**, 102) for acetic acid; β is constant within the accuracy of measurement irrespective of chain length, and has the value 29·6. The curves for *iso*amyl, *sec.*-octyl, and *tert.*-hexyl (1 : 1-dimethylbutyl) alcohols are superimposed as broken lines in Fig. 1 for comparison. Each alcohol is less surface-active than the corresponding straight-chain alcohol. The β values for *iso*amyl and *sec.*-octyl alcohols differ only a little from the straight-chain primary alcohol values, but β for *tert.*-hexyl alcohol falls to about 22. When (1) is combined with the approximate form of the Gibbs equation, *viz.*, $\Gamma \doteq -(C/\boldsymbol{R}T)\mathrm{d}\gamma/\mathrm{d}C$, then Γ_∞ approximately $= \beta/\boldsymbol{R}T$. The limiting amount of adsorbate which can be accommodated on the surface at these higher concentrations will diminish as complexity in the structure of the carbon chain increases the molecular cross-section, and thus the β values for these three alcohols are in general agreement with this theory.

FIG. 2.



Szyszkowski's empirical equation (*Z. physikal. Chem.*, 1908, **64**, 385)

$$\gamma/\gamma_0 = 1 - B \log (C/a + 1) \quad . \quad . \quad (2)$$

can be written in the form

$$\gamma = \gamma_0(1 + B \log a) - \gamma_0 B \log C \quad . \quad (3)$$

for the higher concentrations over which Milner's equation holds. Hence $\beta = \gamma_0 B$, and $B = 0{\cdot}407$. This agrees closely with the value 0·411 found by Szyszkowski for the fatty acids, and is consistent with the slightly larger area occupied by the alcohol molecule in a condensed insoluble film at zero compression, *i.e.*, 21·6 sq. A. per molecule compared with 20·5 for the fatty acids (Adam, "Physics and Chemistry of Surfaces," Oxford Univ. Press, 2nd Ed., p. 50). The value of a in (2) varies with concentration, and is only approximately a constant for a given alcohol. Since the surface tensions of the pure alcohols themselves are similar, the values of a must approach a standard figure irrespective of chain length as the percentage concentration approaches 100. After a slight rise at great dilution, a falls as the concentration increases, and this fall would be exaggerated by the introduction of an activity coefficient. The values of a have been determined for each *n*-alcohol at 20° over the available concentration range, and are given in Fig. 2. For chains of more than four carbon atoms, the final rapid rise in a is not obtained because of the solubility barrier, but a uniform system clearly holds throughout. The peak values of a which occur at low concentration have been used as a basis on which to compare the alcohols, and are listed in Table I, col. 2, together with the values reported by Szyszkowski for fatty acids of equal chain length (col. 4). The short-chain alcohols are a little more surface-active than the acids of equal chain length because of the enhanced water solubility of the carboxyl group, but increase in chain length will minimise this effect. Thus it is reasonable that the a values for the shorter-chain alcohols should be lower than those for the corresponding acids, but approach the acid value at greater chain length. This is found to be the case; and the ratios of the values of a for alcohols differing by one carbon atom are a little below that for the acids. Agreement with Traube's rule has been confirmed by measuring the con-

TABLE I.

C atoms in *n*-alcohol molecule.	a.	a_n/a_{n-1}.	a for acid molecule (Szyszkowski).	a_n/a_{n-1} (Szyszkowski).	Molar concn. at 55 dynes/cm.	$C_n\ C_{n-1}$.
1	1·290	—	—	—	3·16	—
2	0·400	3·24	—	—	1·05	3·02
3	0·126	3·16	0·165	—	0·316	3·31
4	0·0407	3·09	0·051	3·24	0·100	3·16
5	0·0135	3·02	0·015	3·40	0·0309	3·24
6	0·00447	3·02	0·0043	3·49	0·0100	3·09
7	0·00135	3·31	—	—	0·00295	3·39
8	0·000407	3·31	—	—	0·000832	3·39
		Mean 3·16		Mean 3·38		Mean 3·23

centration of each alcohol required to lower the surface tension to 55 dynes/cm. These values are quoted in col. 6, and the ratios for alcohols differing by one carbon atom (col. 7) are in quite close agreement with the *a* ratios.

The results in Table I confirm that the increase in surface activity with chain length is regular for the alcohols used at the higher concentrations. However, the dynamic studies must frequently be restricted to dilute solutions, and this regularity has been shown to extend to infinite dilution by determining the work of adsorption for each alcohol. Langmuir (*J. Amer. Chem. Soc.*, 1917, **39**, 1883 *et seq.*) has shown that the work done in transferring 1 g.-mol. of the solute from the bulk of the liquid to the surface increases for each additional carbon atom in accord with the equation

$$\lambda_n - \lambda_{n-1} = \boldsymbol{R}T \log (\Gamma/\tau C)_n/(\Gamma/\tau C)_{n-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where τ is the thickness of the surface layer. The mean value of C_n/C_{n-1} given in Table I, when substituted into this equation, gives $\lambda_n - \lambda_{n-1} = 687$ cals. per g.-mol.

The work of adsorption λ has been calculated from the Langmuir equation

$$\lambda = \boldsymbol{R}T \log \Gamma/\tau C \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

the thickness of the surface layer being assumed to be 6 A. throughout. λ is a constant property of any given adsorbate so long as Γ is proportional to C, which is the case in very dilute solutions only. The Γ–C curve was therefore determined separately for each alcohol, and the value of Γ/C obtained from the slope of the tangent to this curve at the origin. The values of Γ/C, and λ deduced therefrom, are given in Table II. The values of λ were substituted into the equation

$$\lambda = \lambda_0 + \kappa n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where n is the number of carbon atoms in the molecule and κ is a constant. It has been found that λ_0 varies appreciably if the value of $\lambda_n - \lambda_{n-1}$ obtained from equation (4), *i.e.*, 687 cals./g.-mol., is substituted for κ in equation (6). Langmuir (*loc. cit.*) found for a number of series that λ_0 was reasonably constant if $\kappa = 625$,

TABLE II.

C atoms in *n*-alcohol molecule.	Γ/c, cm. × 10^6.	λ, cals./g.-mol.	λ_0, cals./g.-mol.	C atoms in *n*-alcohol molecule.	Γ/c, cm. × 10^6.	λ, cals./g.-mol.	λ_0. cals./g.-mol.
1	0·45	1180	555	5	36·0	3750	625
2	1·32	1810	560	6	105	4380	630
3	4·00	2460	585	7	300	4990	616
4	11·20	3070	570	8	900	5630	630

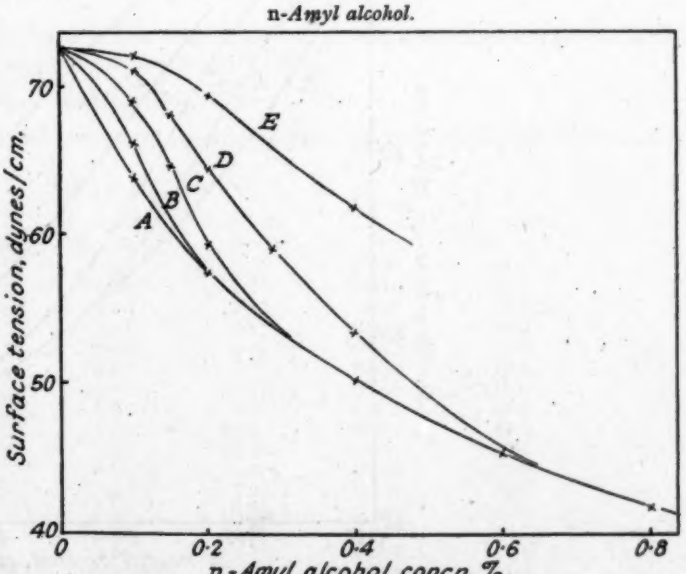
and this value has been used in determining λ_0 (Table II, col. 4). The small increase in λ_0 with chain length is not significant in view of the calculation errors involved. The mean value is 597 cals./g.-mol., in good agreement with Langmuir's primary alcohol value of 575.

Dynamic Surface Tensions.—An attempt has been made to determine the migrational velocity of each alcohol by measurement of the vibrating jet formed from the aqueous solution. The plate orifice described elsewhere (Addison, *Phil. Mag.*, in press) was used, with a mean orifice radius of 0·055 cm. Variation in wave-length due to turbulent flow was thus restricted to the first wave. The head of pressure on the orifice was adjusted, to a degree depending on the density of the test liquid, in order to maintain the flow rate constant throughout at 1·99 ml./sec.

With methyl, ethyl, *n*-propyl, and *n*-butyl alcohols, no variation in wave-length after the first wave was apparent at any concentration; the measurement of dynamic tensions for these alcohols in aqueous solution is therefore beyond the scope of the vibrating-jet method. The migrational velocity is a direct ratio between the distance travelled by the adsorbate molecules and the time taken, and if the concentration of these first members of the series is decreased until the time taken is large enough to be measurable in the jet, the equilibrium surface tension of the solution is so near to the pure water value that the variation in wave-length in

FIG. 3.

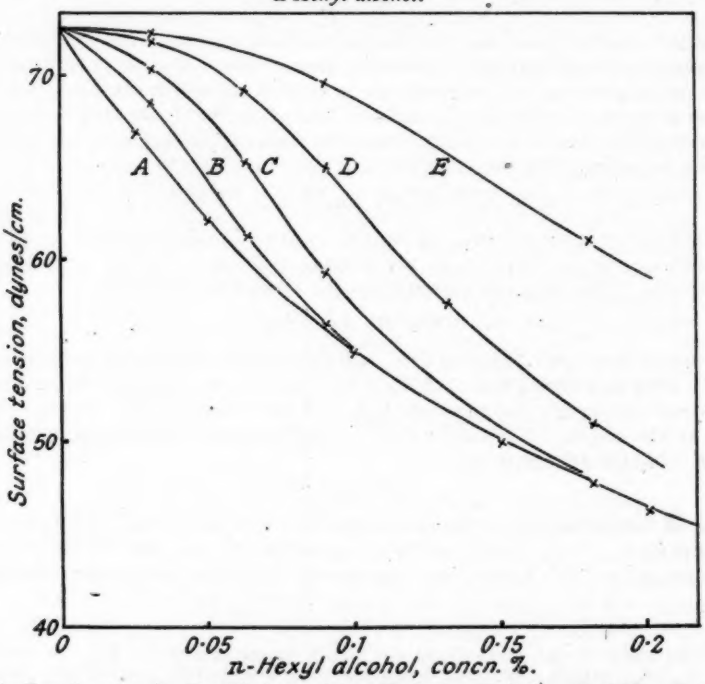
n-Amyl alcohol.



Surface age (secs.): A, *Equilibrium curve.* B, 0·016. C, 0·012. D, 0·008. E, 0·005.

FIG. 4.

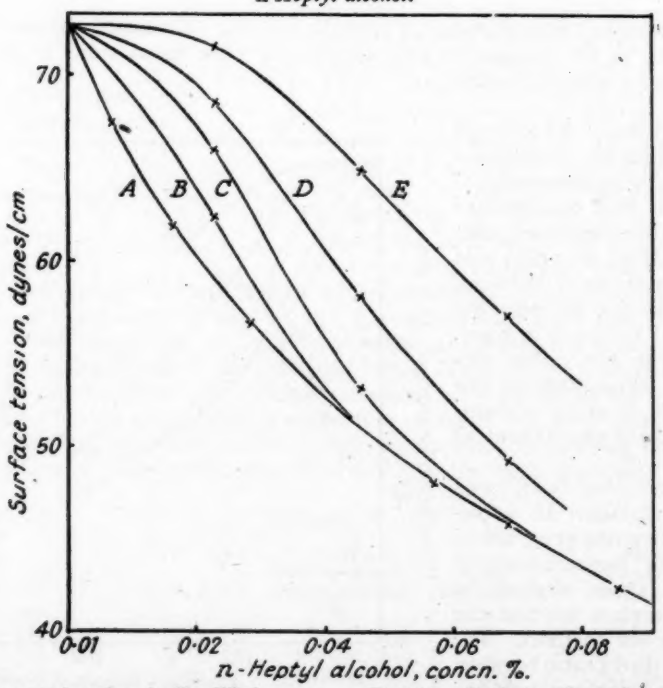
n-Hexyl alcohol.



Surface age (secs.): A, *Equilibrium curve.* B, 0·06. C, 0·02. D, 0·01. E, 0·005.

FIG. 5.

n-Heptyl alcohol.

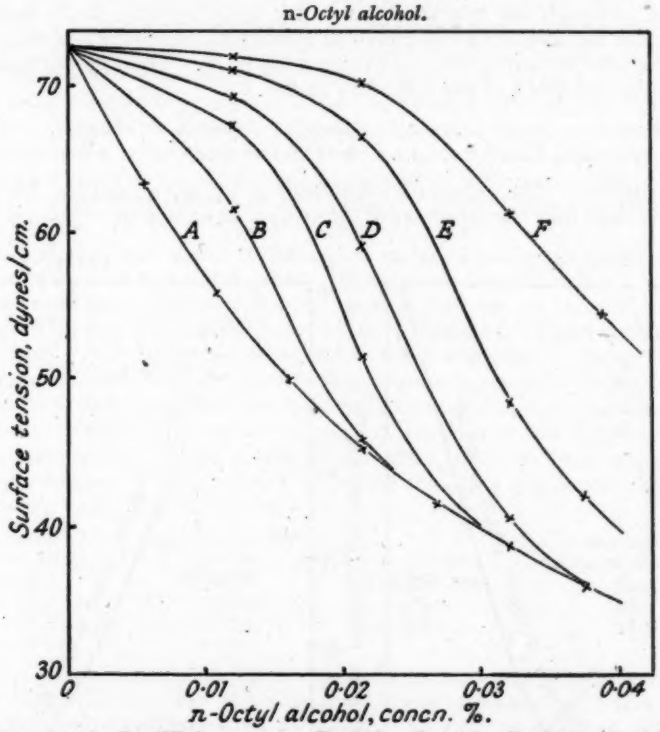


Surface age (secs.): A, *Equilibrium curve.* B, 0·05. C, 0·03. D, 0·02. E, 0·01.

the jet is within the experimental error of measurement. As the chain length is increased, the range of surface tension available with the dilute solutions is also increased, so that the wave-length varies along the jet to a measurable degree. This is first apparent with amyl alcohol, and change in wave-length is progressively more

pronounced as chain length increases. Surface tension–concentration curves at 20° for *n*-amyl, -hexyl, -heptyl, and -octyl alcohols at various surface ages are recorded in Figs. 3—6. In contrast to the behaviour of the methyl–butyl alcohols, the minimum concentration of *n*-octyl alcohol required to give an accurately measurable change in wave-length is so small (and thus the distance from which adsorbate is drawn is so large) that equilibrium is not established before break-up of the jet.

FIG. 6.



Surface age (secs.) : A, *Equilibrium curve.* B, 0·10. C, 0·06. D, 0·04. E, 0·02. F, 0·01.

Migrational Velocities.—The measurements recorded in Figs. 3—6 have been used to calculate the mean velocities of migration to the surface (V) by using the relation (Part II)

$$V = -100M(d\gamma/dC)/KTt$$

Relevant figures are listed in Table III, and the *tert.*-hexyl results are included for comparison with *n*-hexyl alcohol.

TABLE III.

Alcohol.	C, %.	$-d\gamma/dC$.	$\Gamma \times 10^8$, g./cm.^{2}.	$d \times 10^5$, cm.	t, secs.	$V \times 10^4$, cm./sec.
n-Amyl	0·10	65	2·35	2·35	0·023	10·2
	0·20	45	3·25	1·62	0·016	10·1
	0·40	32	4·62	1·15	0·012	9·6
n-Hexyl	0·03	206	2·59	8·63	0·055	15·7
	0·06	154	3·86	6·43	0·041	15·7
	0·09	120	4·52	5·02	0·034	15·0
	0·12	100	5·01	4·17	0·026	15·9
	0·18	80	6·03	3·35	0·023	14·6
n-Heptyl	0·02	520	4·95	24·7	0·074	33·5
	0·04	340	6·47	16·2	0·048	32·8
	0·06	240	6·85	11·4	0·037	31·1
	0·08	188	7·16	8·95	0·029	30·6
n-Octyl	0·0224	800	9·55	42·7	0·068	62·8
	0·030	650	10·40	34·7	0·052	66·7
tert.-Hexyl	0·06	98	2·46	4·10	0·035	11·6
	0·09	75	2·82	3·14	0·028	11·2
	0·14	54	3·16	2·26	0·019	12·0

The mean value of V for each alcohol is plotted against the chain length in Fig. 7. The failure of the practical technique sets the lower limit for the *n*-alcohols at five carbon atoms. Above eight carbon atoms, the solubility is so small that, although an appreciable range of surface tension is available with saturated

solutions of nonyl and decyl alcohols, equilibrium is not established, even with saturated solutions, before the end of the jet. These systems can be used for the determination of true rates of migration during a part of the total time required for equilibration (see Part III), but a method capable of measuring a wider range of surface ages is needed before the time to equilibrium, and thus the migrational velocity, can be determined. However, from the smooth curve drawn through the available *n*-alcohol values it is clear that dV/dn increases rapidly with increasing chain length. The curve can be extrapolated to give migrational velocities of neighbouring alcohols with fair accuracy.

It is of interest that, although the migrational velocity increases with chain length, the time t taken to establish equilibrium under the available experimental conditions also increases with chain length, since the solubility diminishes at a rate exceeding the rate of increase of V. The approximate times are given below for concentrations equal to one-tenth of the solubility at 20°.

n-Alcohol	Amyl.	Hexyl.	Heptyl.	Octyl.
t (sec.)	0·015	0·035	0·07	>0·1

Influence of Chain Structure.—The values of V for *iso*amyl, *sec.*-octyl, and *tert.*-hexyl alcohols are included in Fig. 7, from which it is clear that the structure of a molecule has a definite effect on its migrational velocity.

FIG. 7.

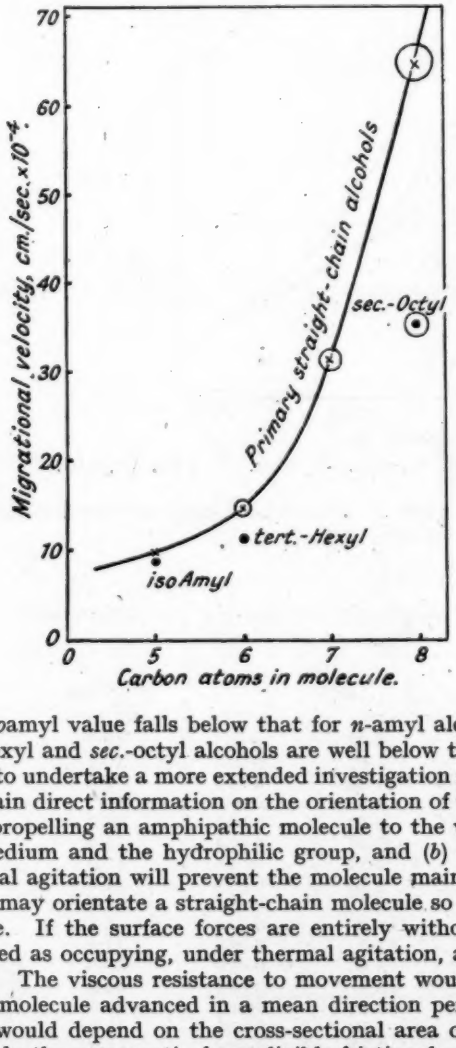
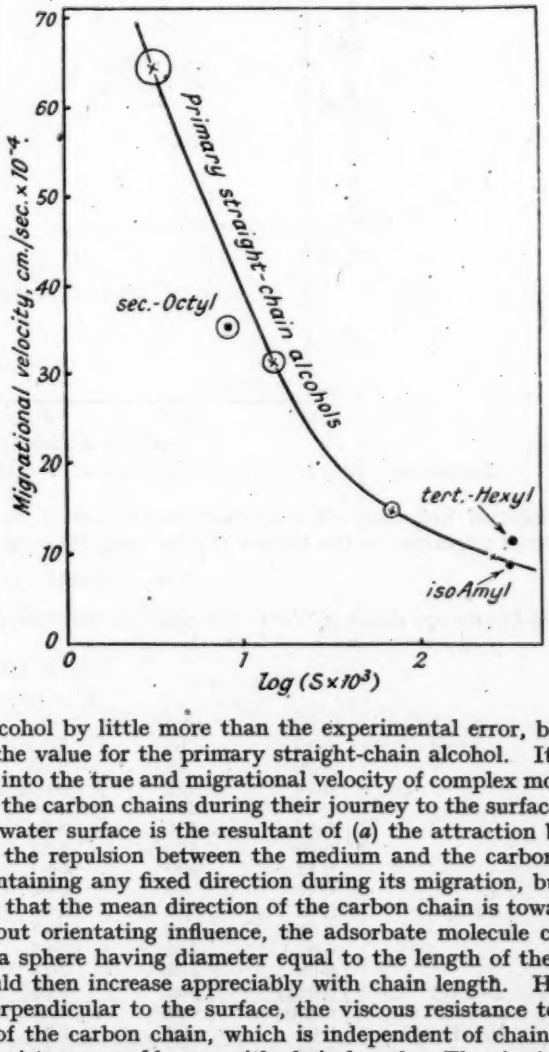


FIG. 8.



The *iso*amyl value falls below that for *n*-amyl alcohol by little more than the experimental error, but both *tert.*-hexyl and *sec.*-octyl alcohols are well below the value for the primary straight-chain alcohol. It is proposed to undertake a more extended investigation into the true and migrational velocity of complex molecules, to obtain direct information on the orientation of the carbon chains during their journey to the surface. The force propelling an amphipathic molecule to the water surface is the resultant of (*a*) the attraction between the medium and the hydrophilic group, and (*b*) the repulsion between the medium and the carbon chain. Thermal agitation will prevent the molecule maintaining any fixed direction during its migration, but these forces may orientate a straight-chain molecule so that the mean direction of the carbon chain is towards the surface. If the surface forces are entirely without orientating influence, the adsorbate molecule could be regarded as occupying, under thermal agitation, a sphere having diameter equal to the length of the carbon chain. The viscous resistance to movement would then increase appreciably with chain length. However, if the molecule advanced in a mean direction perpendicular to the surface, the viscous resistance to movement would depend on the cross-sectional area of the carbon chain, which is independent of chain length, and only the comparatively negligible frictional resistance would vary with chain length. The rise in migrational velocity with chain length found experimentally does not in itself provide proof of orientation, for if the solubility of the alcohols in water be taken as some measure of the repulsive forces operating on the carbon chain, it is probable that the forces propelling the carbon chain increase at a much greater rate than the viscous resistance to unorientated movement. The branching of the carbon chain would probably have

little effect in the absence of orientation, but might be expected to reduce appreciably the velocity of an orientated molecule. Also, the orientating influence would be diminished as a result of the transfer of the hydrophilic group from the end to some other position in the chain. A knowledge of the actual forces operating on the alcohol molecule is therefore necessary to determine where between the two limits the actual orientation lies. This force is being determined from the acceleration of the alcohol molecules which takes place when the free surface energy first operates (see Part III) and this will be the subject of further communications.

The structure of each of the three alcohols is such that the centres of hydrophobic and hydrophilic attraction are closer than in the straight-chain alcohol. The solubilities in water are therefore greater, and the forces promoting migration are less, than for the straight-chain alcohol of equal carbon content, and it seemed possible that this effect alone might account for the smaller velocities. If such were the case, all the alcohols should lie on the same velocity–solubility curve. The information available in the literature on the solubilities of the alcohols above amyl is meagre, and the solubilities have therefore been determined on the actual samples used in the tension measurements. Because of the low order of solubility, it was not possible to determine visually whether a drop of the alcohol added to a large volume of water dissolved during stirring, or remained attached to the walls of the vessel as a separate phase. The surface tension of the solutions was therefore utilised as follows.

Sufficient excess of the alcohol was added to 100 ml. of water in a stoppered flask to form a separate lens on the surface. The mixture was then swirled gently (too vigorous agitation gave a semi-permanent emulsion which upset the tension readings). After settling, a small sample of the clear aqueous solution was withdrawn into a drop weight pipette, and the surface tension determined. The swirling was continued until a steady tension was obtained. The tension–concentration curve was known, and required only slight extrapolation (the logarithmic scale was very convenient) to the concentration corresponding to the steady saturation tension. It should be stated here that, before static or dynamic tension measurements were commenced on any of the alcohols above amyl, the surface tension at saturation was determined. The concentrated stock solution was then prepared by adding a weighed quantity of the alcohol to a known volume of water, and stirring until a steady tension was obtained. Provided that this was higher than the saturation value, the absence of undissolved alcohol was confirmed.

Alcohol.	γ of saturated solution, dynes/cm.	Solubility at 20°, % w/w.	Alcohol.	γ of saturated solution, dynes/cm.	Solubility at 20°, % w/w.
n-Amyl	28·2	2·21	*iso*Amyl	26·8	2·66
n-Hexyl	29·9	0·706	*tert.*-Hexyl	30·0	3·23
n-Heptyl	31·6	0·172	*sec.*-Octyl	34·1	0·106
n-Octyl	33·4	0·042			

The solubilities of the seven alcohols on which dynamic measurements have been made, determined by the above method, are listed above. For the *n*-alcohols there is an almost linear relation between chain length and the surface tension of the saturated solution. The relation between solubility and migrational velocity is plotted in Fig. 8, where S = solubility in g.-mol./l. *iso*Amyl alcohol can be regarded as lying almost on the smooth curve given by the *n*-alcohols, but both *sec.*-octyl and *tert.*-hexyl alcohols still lie well away from the curve. Therefore when the structure of an alcohol of given carbon content is altered, other factors in addition to the solubility factor operate to alter the migrational velocity. If the carbon chains are orientated towards the surface during adsorption, complexity of structure and the position of the hydrophilic group will also influence the rate of adsorption, and may explain these results. These possibilities are being studied further.

Experimental.

Limits of Experimental Error.—Where surface tensions have been measured by the drop-weight method, high accuracy (to at least 0·1 dyne/cm.) is achieved. Where the vibrating jet and the simplified mathematical treatment given in Part I have been used, the results are considered to be accurate to $\pm$ 0·25 dyne. Since the tensions measured have been of the order of 40—70 dynes, the error does not exceed $\pm$ 0·6%, and is not significant in Figs. 1—6. The surface ages recorded in Figs. 3—6 are obtained by direct linear measurement of the jet, with an accuracy of 0·01 cm. The possible error is thus of the order of $\pm$ 0·5% at the beginning of the jet but becomes negligible at higher surface ages. The solubilities reported above are based on drop-weight measurements of surface tension, and are therefore regarded as being of the same high order of accuracy.

The experimental error becomes more significant in considering the migrational velocities, particularly where small differences in velocity are compared. Since V is a function of $(d\gamma/dC)/t$, the percentage error in V may be as high as the sum of the maximum errors in $d\gamma/dC$ and t. $d\gamma/dC$ is obtained from the equilibrium γ–C curve, which can be obtained accurately from drop-weight measurement. Errors in reading the slope of the tangent at any particular concentration can be minimised by smoothing the $d\gamma/dC$–C curve, and it is considered that the error in the reported values of $d\gamma/dC$ nowhere exceeds 1%. The greatest source of error lies in the measurement of t, since the rate of change of tension falls rapidly as surface equilibrium is approached. Again, measurement is least accurate with the weaker solutions, *i.e.*, at greater surface ages, and the possible error increases up to about 0·0025 sec. at surface ages of 0·08—0·10 sec. Thus the maximum experimental error in the determination of V from a single measurement may rise to $\pm$ 3%, although this error may be reduced by increasing the number of determinations at a given concentration. The results in Table III (and Parts II and III) indicate that values of V for a given alcohol over a range of concentrations may occasionally vary up to $\pm$ 5%. It is possible that some physical cause (so far undetermined) may be partly responsible for this wider variation. However, for present purposes the whole of this variation has been assumed to be due to experimental error, and is the basis on which the experimental error in Figs. 7 and 8 has been assessed. The limits of error are indicated for convenience by the size of the points (or by circles drawn round the points where the error is sufficiently large), without implying any error in the horizontal axis.

Purity of Alcohols.—Neither density nor refractive index alone was reliable as a measure of purity. Boiling point provides a more sensitive index, and the purity of each alcohol was assessed by measurement of all three physical properties. The refractive index was determined by an Abbé refractometer, sodium light being used. In some cases the pure alcohols supplied required no further purification; impure alcohols were purified by fractional distillation. The middle fraction from a normal distillation was redistilled through a fractionating column, and the appropriate fraction collected. In some cases this fraction, although of correct b. p., gave a density and/or refractive index differing appreciably from published values. Azeotrope formation was regarded as probably reponsible, and a number of samples were rejected for this reason. Samples were not used for the adsorption measurements until all three properties were in suitable agreement with published values; measured values on the samples used are given below.

Alcohol.	$d_4^{20°}$.	B. p.	$n_D^{20°}$.	Alcohol.	$d_4^{20°}$.	B. p.	$n_D^{20°}$.
Methyl	0·7924	65·0°	1·3294	*n*-Heptyl	0·8220	176·5°	1·4241
Ethyl	0·7898	78·5	1·3610	*n*-Octyl	0·8244	194·5	1·4291
n-Propyl	0·8040	98·0	1·3856	*iso*Amyl	0·8127	131·5	1·4075
n-Butyl	0·8101	118·0	1·3993	*tert.*-Hexyl	0·8048	122·0	1·4120
n-Amyl	0·8154	138·0	1·4102	*sec.*-Octyl	0·8200	178·0	1·4255
n-Hexyl	0·8194	157·5	1·4182				

The author's thanks are due to the University of Durham (Durham Division) and to Imperial Chemical Industries Ltd. for the gift of some of the alcohols used in this work.

HARRIS INSTITUTE TECHNICAL COLLEGE, PRESTON. [*Received, November 2nd,* 1944].

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27. *Experiments on the Interaction of Hydroxy-compounds and Phosphorus and Thionyl Halides in the Absence and in the Presence of Tertiary Bases. Part II.*

By WILLIAM GERRARD.

Although the interaction of phosphorus oxychloride and (+)β-octanol yielded evidence of the formation of the chlorophosphates, $POCl_2 \cdot OR$ and $POCl(OR)_2$, it appears most probable that the pre-ionisation and internal decomposition of these are not responsible for the formation of any chloride, RCl, in the system. In the presence of pyridine, the behaviour of this alcohol is closely analogous to that of *n*-butyl alcohol (Gerrard, J., 1940, 1464).

Neither in the absence nor in the presence of pyridine was there any evidence of formation of chlorophosphates or phosphoric esters from (−)phenylmethylcarbinol; the chloride, RCl, was formed from the beginning of each operation.

Ethyl (−)mandelate, in the absence of pyridine, gave neither the chloride, RCl, nor chlorophosphates; but in the presence of pyridine, its behaviour may be described as intermediate between that of the other two hydroxy-compounds.

It is suggested that mechanisms comprising " end-on " and " broadside " oriented collisions appear in these systems; these are regarded as more probable than those involving the pre-ionisation of " intermediate " chloro-esters.

IN this experimental survey of the interaction of optically active β-octanol, phenylmethylcarbinol, or ethyl mandelate with phosphorus oxychloride in the absence and in the presence of pyridine, an attempt has been made to disentangle conditional and structural factors and to reveal possibilities of still further analyses by kinetic methods.

When (+)β-octanol was mixed with the oxychloride at 15° there was no immediate evolution of hydrogen chloride, but a subsequent slow reaction evolved this gas and afforded a mixture of (−)β-octyl chloride, the chlorophosphates $POCl_2 \cdot OR$ and $POCl(OR)_2$, and the ester, $PO(OR)_3$. It is believed that the chloride, RCl, was formed concurrently with the chlorophosphates, and not by a unimolecular decomposition or by subsequent ionisation of these. These chlorophosphates could not be isolated in a pure state, as was done with the *n*-butyl compounds (Gerrard, *loc. cit.*) and with the β-octyl chlorophosphites (Part I, J., 1944, 85), but the corresponding phosphoric esters were obtained by hydrolysis. The chlorophosphates were slowly formed by the interaction of the oxychloride and the ester $PO(OR)_3$; but no more than a trace of chloride, RCl, could be obtained by the specified treatment of these mixtures.

(−)Phenylmethylcarbinol and the oxychloride reacted slowly at 0° without the evolution of hydrogen chloride, and the products were (+)α-chloroethylbenzene and a residue which did not contain phosphoric esters (cf. Kenyon, Phillips, and Taylor, J., 1931, 382). There was not the slightest indication of the formation of chlorophosphates.

Ethyl (−)mandelate and the oxychloride interacted slowly, even at 60°, and produced neither the chloride, RCl, nor phosphoric esters; the highly viscous mass obtained as a residue was not further examined. Thionyl chloride (Part I, *loc. cit.*) gave rise to the chlorosulphinate, and phosphorus trichloride (*ibid.*) to the chlorophosphites.

The use of pyridine in the reaction with (+)β-octanol had two functions. Addition of the oxychloride (⅓ mol.) to the mixture of alcohol (1 mol.) and base (1 mol.) resulted in nearly theoretical yields of pyridine hydrochloride and the ester, $PO(OR)_3$. Continued addition of the oxychloride then converted, under favourable conditions, the ester into a mixture of chlorophosphates, which did not yield the chloride, RCl, in the presence of the pyridine hydrochloride, although when free pyridine was present, the mixture gave the chloride, RCl, in strict analogy with the example of *n*-butyl alcohol (Gerrard, *loc. cit.*). Houssa and Phillips (J., 1932, 108),

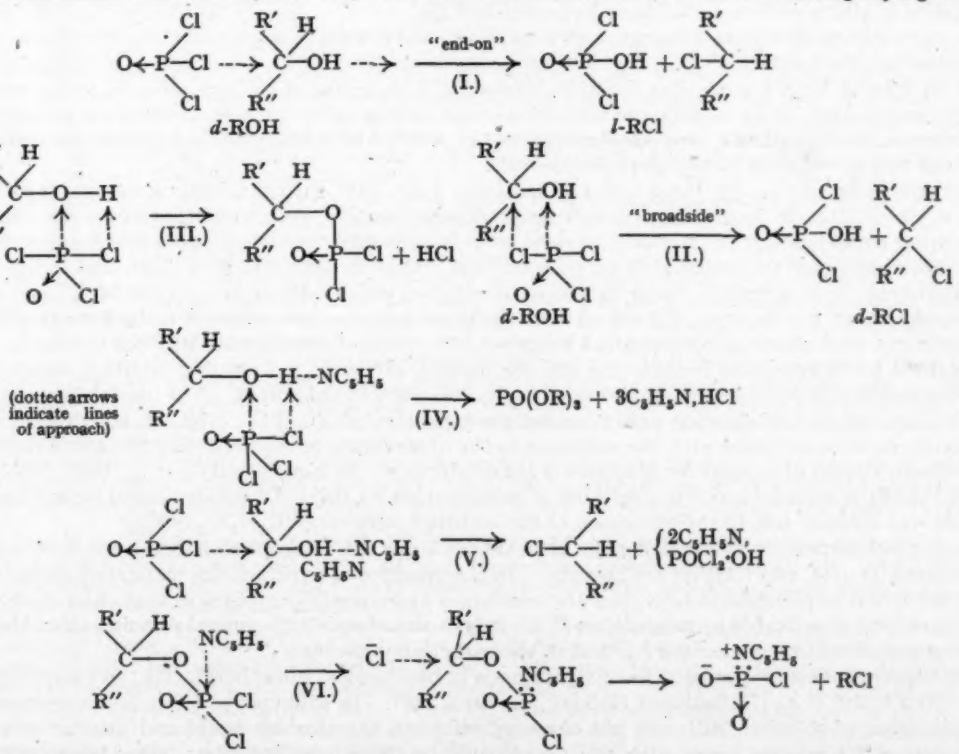
from the oxychloride (1 mol.), β-octanol (1 mol.), and pyridine (2 mols.) in ethereal solution, obtained ultimately only phosphoric esters.

The white solids precipitated when pyridine was added to the reaction mixture of alcohol and oxychloride, or of the tri-ester and oxychloride, were essentially phosphorus compounds, probably mixed with pyridine hydrochloride, and resulted from the interaction of pyridine with the products of reactions that had already occurred. Analytical results indicated the ratio $2C_5H_5N : POCl_2{\cdot}OH$. The precipitate could not be due to unchanged oxychloride, because this compound and pyridine when mixed in dry ethereal solution formed only a trace of precipitate, and none at all in absence of ether.

(−)Phenylmethylcarbinol gave no sign of phosphoric ester formation, even in presence of pyridine. Addition of oxychloride to the mixture of alcohol and base in ethereal solution at 0° caused production of (+)α-chloroethylbenzene from the beginning, and the precipitate formed at the same time had a composition represented by 2Cl, $2C_5H_5N$, P, and probably 2O. The rotatory power of the chloride, RCl, increased as the proportion of pyridine was increased.

Ethyl (−)mandelate, when mixed with pyridine in ethereal solution and then treated with phosphorus oxychloride, yielded both ethyl (+)phenylchloroacetate and phosphoric esters from the beginning of the reaction. Increase in the proportion of oxychloride increased the proportion of the chloroacetate with respect to the phosphoric ester, and in absence of ether, from (−)mandelate (1 mol.), pyridine (1 mol.), and oxychloride (1 mol.) an excellent yield of (+)chloroacetate was produced. It is remarkable that for more than ½ mol. of the oxychloride, the analytical data for the precipitate are similar to those stated for the other two hydroxy-compounds. Wagner-Jauregg (*Helv. Chim. Acta*, **1929**, **12**, 61) showed that pyridine facilitated formation of the chloride, RCl, from methyl mandelate, 2 mols. of pyridine for 1 mol. of each of the other compounds being used. An interesting comparison is afforded by Fischer and Pfahler (*Ber.*, 1920, **53**, 1606), who showed that even at −20° phosphorus oxychloride and pyridine converted ethylene glycol into chloroethyl dihydrogen phosphate.

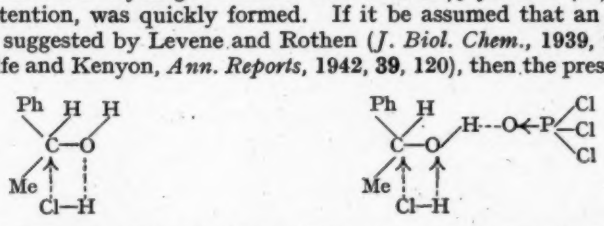
It is now suggested that the observations reported may be explained in terms of mechanisms involving oriented collisions either " end-on " (inversion) or " broadside " (retention), as in the accompanying scheme.



With (+)β-octanol in absence of ether, mechanisms (I) and (III) predominate, although (II) proceeds to some extent and reduces the rotatory power of the (−)chloride, RCl, formed. In presence of pyridine (1 mol.), (IV) will proceed, and if sufficient oxychloride is used, the chlorophosphates will be formed from the tri-ester, and in the presence of free base mechanism (VI) (cf. Kenyon, Phillips, and co-workers) can then operate. Inversion without loss of rotatory power is to be expected from (IV) and (VI), and this is supported by experiment.

(−)Phenylmethylcarbinol is converted into (+)chloride, RCl, entirely by mechanisms (I) and (II), (I) predominating but (II) being quite large and giving rise to considerable loss of activity. In the presence of pyridine, there is a strong tendency for (V) to proceed exclusively; but if there is insufficient pyridine present,

some alcohol molecules will be denuded (2 molecules of pyridine are precipitated for each phosphorus atom) and will come under the influence of mechanisms (I) and (II). The production of (+)α-chloroethylbenzen having a high rotatory power is therefore explained. When the (−)alcohol ($\alpha_D^{16°}$ −18·4°) was added to the oxychloride stirred by a current of hydrogen chloride at 0°, an 80% yield of (−)α-chloroethylbenzene ($\alpha_D^{16°}$ −2·8°), predominating retention, was quickly formed. If it be assumed that an addition compound (VII) is formed, similar to that suggested by Levene and Rothen (*J. Biol. Chem.*, 1939, **127**, 237) for the action of hydrogen bromide (cf. Balfe and Kenyon, *Ann. Reports*, 1942, **39**, 120), then the presence of oxychloride and/or

(VII.) 

the reaction product, $POCl_2 \cdot OH$, may facilitate removal of water and give the retention reaction an advantage. There is, however, another possibility depending on the facilitation of the broadside collision by the formation of a hydrogen bond, ROH . . . . O←PCl_3. This is not unlikely, for Audrieth and Steinman (*J. Amer. Chem. Soc.*, 1941, **63**, 2115) have shown that, whereas the heat of mixing of the oxychloride and chloroform was 482 cals./g.-mol. probably indicative of hydrogen bond formation, CCl_3H . . . O←PCl_3, yet there was no heat effect when the oxychloride was mixed with carbon tetrachloride. Indeed, there appears to be no reason for excluding the influence of the hydrogen bond on mechanisms (I) and (II).

The author does not exclude the possibility of pre-ionisation, suggested by the work of Kenyon and Phillips (*Trans. Faraday Soc.*, 1930, **26**, 451; cf. Arcus, J., 1944, 236) and Hughes and Ingold (J., 1937, 1252) and their respective co-workers; but it is necessary to point out that Hughes and Ingold's experiments were conducted on the hydrolysis of halides, RX, under conditions very different from those existing in the systems now considered. Those experiments of Kenyon and Phillips which appear to be comparable with those of Hughes and Ingold were conducted in hot alcoholic solution and involved the interaction of toluene-*p*-sulphonic esters with alkali salts of either carboxylic acids or hydrogen halides.

In the view of Bateman, Hughes, and Ingold (J., 1944, 243) it is still not known whether, or in what circumstances, the formation of an organic chlorosulphinate, R·O·SOCl, is a single or a composite process. It might be formed by a bimolecular reaction between the molecule of thionyl chloride and a molecule of the hydroxy-compound, or by a slow pre-ionisation stage, followed by a rapid association of appropriate ions. Nevertheless, in the author's view (cf. Part I) there appears to be nothing against the mechanism involving the broadside collision similar to that depicted in (III).

The conclusion drawn by Boyd and Ladhams (J., 1928, 215) with the implication of generality, that the function of pyridine in facilitating phosphoric ester and chloride, RCl, formation is due to the reactivity of an addition compound, $2C_5H_5N,POCl_3$, stands very precariously even on their own experiments with diary oxy*iso*propyl alcohols. Considerable excesses of base and of oxychloride were used, and it was necessary to use chloroform as a solvent in order to obtain a complex which with water gave a 96% yield of the mono-phosphoric ester; but in a parallel experiment the same complex was assumed to be formed without the use of chloroform, and when the complex was heated, a 77% yield of the chloride RCl was obtained. Chloroform was deemed to be necessary because the effective concentration of the reactive addition compound, reduced by its insolubility in pyridine, was maintained by its solubility in chlorofom. The insolubility of their addition compound in carbon tetrachloride would suggest the formation of CCl_3H . . . NC_5H_5 and CCl_3H . . . O←PCl_3 in chloroform, in accordance with the reference to the observation of Audrieth and Steinman (*loc. cit.*). Boyd and Ladham's claim of support by analogies is not established; McKenzie and Gow (J., 1933, 705), for example, believed that the retardation of the velocity of halogenation by thionyl chloride caused by the use of excess of pyridine was actually due to the formation of the addition compound $(C_5H_5N)_2,SOCl_2$.

Since ethyl mandelate gave neither the chloride, RCl, nor the chlorophosphates, it must be concluded that mechanisms (I), (II), and (III) do not operate. In the presence of pyridine, the mandelate resembles β-octanol in the formation of phosphoric ester, but also resembles phenylmethylcarbinol in that chloride, RCl, is formed from the outset, presumably by mechanism (V). It is in accordance with general principles that the effect of the phenyl group should be moderated by that of the carbethoxyl group.

The experiments now discussed have significance in biochemical phosphorylation, and may explain the low yields often found (*e.g.*, Gulland and Hobday, J., 1940, 746). In Plimmer and Burch's experiments (J., 1929, 279) formation of chloride, RCl, was not observed although the alcohols (cetyl and chloroethyl; cholesterol) were refluxed for several hours with the oxychloride in chloroform solution; after treatment with water, phosphoric esters were obtained. An attempt to prepare cetylphosphoryl chlorides by heating molecular proportions for 6 hours led to the isolation of cetene only. They could not repeat the experiment of Euler and Bernton (*Ber.*, 1927, **60**, 1721), who reported an unspecified yield of mono- and di-ester (no mention being made of chloride formation) from the action of the oxychloride on cholesterol in the presence of pyridine. Plimmer and Burch appeared to prefer the use of oxychloride alone.

The work now described has also an essential bearing on the interaction of hydroxy-compounds and phosphorus pentachloride; for if the primary reaction is $PCl_5 + ROH \longrightarrow RCl + POCl_3 + HCl$, the oxychloride may react on its own account and have a considerable influence on the nature and yields of products.

Experimental.

General Procedures.—The hydroxy-compounds and the oxychloride reacted slowly at 0°, and mixing could be done quickly without appreciable evolution of heat. After the reaction mixture had been kept for the time and at the temperature stated, it was poured on ice and given "aqueous treatment," which comprised extraction of the oil with ether, washing the ethereal solution with a solution of sodium carbonate to extract acid and acid phosphoric esters, acidification (dilute sulphuric acid) of the carbonate solution, and extraction with ether of any acid ester which separated. The two ethereal solutions were separately dried (sodium sulphate) and evaporated. Phosphate and chloride ions were quantitatively determined in the sum of the aqueous liquids in order to follow the fate of the respective elements.

When pyridine was used in ethereal solution, the oxychloride, also in ethereal solution, was added dropwise to an ethereal solution of the hydroxy-compound and base, and after a specified time the liquid was decanted from the white solid and poured on ice. The solid was washed with three small amounts of dry ether, placed in a vacuum for 2 hours, and analysed. The ethereal washings were added to the original ethereal solution and given the aqueous treatment already described. When the operation was conducted in absence of ether, the mixture of the precipitate and liquid was given aqueous treatment. Aqueous liquids were examined quantitatively for pyridine and chloride and phosphate ions. Rotatory powers are expressed for 1 dm.

Interaction of (+)β-Octanol, $\alpha_D^{16°}$ +8·0°, and Phosphorus Oxychloride.—Attempts to prepare pure specimens of the chlorophosphates $POCl_2{\cdot}OR$ and $POCl(OR)_2$ by the method used for the corresponding *n*-butyl compounds and for the chlorophosphites of β-octanol (Part I, *loc. cit.*) were unsuccessful. In a series of trials, the primary product from the addition of alcohol (1 mol.) to oxychloride (2 mols.) was kept for different periods of time at 15°/15 mm., 30—40°/15 mm., or 15°/15 mm. in a desiccator containing solid sodium hydroxide, in the endeavour to remove excess of oxychloride; but octylene was formed and the chlorine content remained high (Found: Cl, 35·0, 35·8, 34·8%, for three different experiments). Very little chloride, RCl, could be obtained by distillation, either before or after aqueous treatment.

In the following series of experiments, (+)β-octanol (3·25 g., 1 mol.) was mixed at 0° with the stated amount of oxychloride.

(1) With oxychloride (0·33 mol.) after 30 mins.' standing at 15° there were obtained (−)β-octyl chloride (0·5 g.), b. p. 63—64°/16 mm. $\alpha_D^{16°}$ −23·1°, $n_D^{19°}$ 1·4256; unchanged alcohol (1·0 g.); a residue (0·35 g.) (Found: P, 7·2%); and from the carbonate solution, a residue (1·3 g.), $\alpha_D^{18°}$ +1·75°, $n_D^{20°}$ 1·4345 (Found: P, 11·4%). The phosphoric esters could not be distilled and were not purified. The phosphorus contents of each of these specimens are recorded to indicate probable constitution and to show the fate of this element. The theoretical values for the tri-, di-, and mono-ester respectively are P, 7·1, 9·6, 14·8%.

(2) With oxychloride (0·5 mol.), after 24 hours at 15°, there were obtained (−)β-octyl chloride (1·3 g.), b. p. 57—59°/13 mm., $n_D^{18°}$ 1·4269, $\alpha_D^{16°}$ −23·8°; unchanged alcohol (0·9 g.); a residue (0·45 g.); and from the carbonate solution, a residue (0·4 g.) (Found: P, 12·3%).

(3) From oxychloride (1 mol.), and 1 hour's standing at 15°/15 mm., there resulted (−)β-octyl chloride (1·05 g.), b. p. 64—66°/17 mm., $\alpha_D^{18°}$ −20·1°, $n_D^{18°}$ 1·4276; unchanged alcohol (0·6 g.); a residue (0·5 g.), $n_D^{20°}$ 1·4380 (Found: P, 6·5%); and from the carbonate solution, a residue (1·15 g.), $n_D^{19°}$ 1·4368 (Found: P, 13·4%) (compare Houssa and Phillips, *loc. cit.*). Distillation of the primary mixture before aqueous treatment did not increase the yield of chloride.

Slow addition of the oxychloride (3·3 g., 0·86 mol.) to the alcohol (3·3 g., 1 mol.) in a stream of carbon dioxide at 0°, followed by standing at 15° for 12 hours and then aqueous treatment, led to the isolation of (−)β-octyl chloride (1·6 g.), b. p. 64°/16 mm., $n_D^{18°}$ 1·4262, $\alpha_D^{18°}$ −24·8°, and a residue (1·3 g.), $n_D^{19°}$ 1·4400. The latter (Found: Cl, 10·0; P, 9·6%) was probably a mixture of the chlorophosphate, $POCl(OR)_2$ (Calc.: Cl, 10·4; P, 9·1%), and the di-ester, $PO(OR)_2OH$ (Calc.: P, 9·6%), aqueous treatment effecting only a slow hydrolysis of the chlorophosphate and slow extraction of the di-ester. The alkaline extract in the aqueous treatment gave a trace of oil on acidification.

Interaction of (+)β-Octanol, $\alpha_D^{16°}$ +8·0°, and Phosphorus Oxychloride in Presence of Pyridine.—With the reagents in ethereal solution at −10° the precipitation of pyridine hydrochloride commenced at the beginning of the dropwise addition of the oxychloride (2·6 g., 0·33 mol.) to the alcohol (6·5 g., 1 mol.) in the presence of pyridine (3·96 g., 1 mol.), and 25 minutes after the mixture had been removed from the cooling bath, 50% of the final amount of precipitate had formed. The rate of precipitation was therefore very much slower than with the trichloride (Part I). After 2 days at room temperature the ethereal solution was filtered from the precipitate (5·6 g.) (Found: Cl, 30·5. Calc.: Cl, 30·7%), and given aqueous treatment. Only a trace of chloride and phosphate ions was found in the wash-water. On evaporation of the ethereal solution, and keeping the residue for 1 hour at 40°/15 mm., (+)*tri-β-octyl phosphate* (6·59 g.), $\alpha_D^{16°}$ +8·8°, $n_D^{13°}$ 1·4380 (Found: P, 7·8. $C_{24}H_{51}O_4P$ requires P, 7·1%), was obtained. This could not be further purified.

With the alcohol (3·25 g., 1 mol.) and the stated molecular proportions of the other reagents, mixed in absence of ether at −10°, the following experiments were conducted.

(1) With oxychloride (0·33 mol.) and pyridine (1 mol.) a semi-solid mass was formed. This was heated for 1 hour at 70—75°, and aqueous treatment then yielded a fair specimen of the tri-ester (2·8 g.), $\alpha_D^{16°}$ +9·3°, $n_D^{13°}$ 1·4400 (Found: P, 7·9%), and the carbonate solution gave no oil on acidification. The aqueous washings contained only a trace of phosphate ions.

(2) With exactly the same procedure, and with oxychloride (1 mol.) and pyridine (1 mol.), octylene (0·3 g.), a residue (1·65 g.), $\alpha_D^{16°}$ +8·0°, $n_D^{13°}$ 1·4434 (Found: P, 10·2%), and from the carbonate solution, a residue (1·7 g.), $n_D^{15°}$ 1·4379 (Found: P, 13·1%), were obtained. Under these conditions pyridine was present as the hydrochloride and this did not facilitate decomposition of chlorophosphate to the chloride, RCl.

(3) With the same procedure, and with the oxychloride (1 mol.) and pyridine (2 mols.), (−)β-octyl chloride (1·2 g.), b. p. 69°/24 mm., $n_D^{18°}$ 1·4305, $\alpha_D^{16°}$ −26·9°, and a residue (1·6 g.), $n_D^{16°}$ 1·4438, $\alpha_D^{16°}$ +13·5° (Found: P, 9·1%), were obtained; but no oil separated when the carbonate solution was acidified. The acid ester, extracted by carbonate solution in (2), was probably the hydrolytic product of the dichlorophosphate, $POCl_2{\cdot}OR$; and it is this dichlorophosphate which in presence of free base in (3) yielded the chloride, RCl. When the primary mixture was kept at 80—90° for 1 hour, a greater yield of chloride (1·6 g.) and a smaller amount of residue (0·8 g.) were formed, presumably owing to conversion of some of the mono- into the di-chloride: $POCl(OR)_2 \longrightarrow POCl_2{\cdot}OR$.

(4) With the same proportions as in (2), but with 1 hour's reaction at 90—100°, the products were β-octyl chloride (0·5 g.), octylene (1·8 g.), and a residue (0·2 g.). The carbonate solution gave no oil on acidification, and the aqueous washings contained substantially all the phosphorus, and 94% of the chlorine in the system. In these circumstances, the dichloro-ester, $POCl_2{\cdot}OR$, yielded octylene and not chloride, RCl.

When more than 1 mol. of pyridine was used, the aqueous solutions contained alkylpyridinium ion and gave a yellow precipitate with an acidified solution of potassium ferrocyanide (Gerrard, J., 1936, 688; cf. also Boyd and Ladhams, *loc. cit.*).

Addition of the alcohol (4·3 g., 1 mol.) to the oxychloride (10·2 g., 2 mols.), followed by warming at 40°/15 mm. for 12 hours in the endeavour to remove excess oxychloride, led to formation of a residue (7·75 g. Calc. for dichlorophosphate: 8·2 g.) (Found: Cl, 35·8%), which with pyridine yielded a white solid (8·5 g.) and a supernatant liquid. The latter

together with the ethereal washings of the solid afforded, after aqueous treatment, octylene and (−)β-octyl chloride (0·55 g.), b. p. 59°/13 mm., $\alpha_D^{18°}$ −27·9°. The solid was not a pure substance (Found: Cl, 23·2; P, 10·2; C_5H_5N, 53·5. Calc. for $POCl_2{\cdot}OH,2C_5H_5N$: Cl, 24·3; P, 10·6; C_5H_5N, 54·1%), and it was probably formed by interactions (i) of the base and dichlorophosphoric acid, $POCl_2{\cdot}OH$, a reaction product, and (ii) of any dichlorophosphoric ester left undecomposed at the time of addition of base, the chloride RCl being the other product of this interaction.

The alcohol (2·65 g., 1 mol.) and oxychloride (2 mols.) were mixed and kept at 15°/13 mm. for 9 hours, and the product (Found: Cl, 34·8%) when treated with pyridine (2·0 g.) in ethereal solution gave a precipitate (4·38 g.) (Found: Cl, 21·7; P, 11·6; C_5H_5N, 42·9%).

The alcohol (2·6 g., 1 mol.) and oxychloride (3·07 g., 1 mol.) were mixed, and after 2 hours at 15° addition of pyridine (1·6 g., 2 mols.) afforded a precipitate (3·65 g.) (Found: Cl, 22·9; P, 10·3; C_5H_5N, 41·2%); from the ethereal extract octylene (0·9 g.), (−)β-octyl chloride (1·1 g.), b. p. 68°/23 mm., $\alpha_D^{18°}$ −25·4°, and a residue (0·45 g.) were obtained. It is interesting to compare these precipitates with that obtained by the interaction of *n*-butoxyphosphoryl dichloride and pyridine (Gerrard, *loc. cit.*), which was partly separated into two solids having Cl, 18·8, 18·7; P, 14·8, 12·7; C_5H_5N, 41·6, 38·0%, respectively.

Effect of Mixing Phosphorus Oxychloride and Pyridine.—Since Boyd and Ladhams (*loc. cit.*) attributed the function of pyridine in their experiments on aryloxy*iso*propyl alcohols to the formation of a reactive addition compound, $POCl_3,2C_5H_5N$, which, they state, is formed as a crystalline solid when the reagents are mixed in ethereal solution, it was necessary to consider in this light the precipitates described in the foregoing. Boyd and Ladhams mixed pyridine (12 g.) and oxychloride (10 g.) in ethereal solution and immediately obtained an oil which soon solidified (7·4 g.) (Found: Cl, 27·8; P, 9·2. Calc. for $POCl_3,2C_5H_5N$: Cl, 34·1; P, 9·9%), but their analysis seems more in accordance with a mixture of the compound $POCl_2{\cdot}OH,2C_5H_5N$ and pyridine hydrochloride, which could be due to the adventitious absorption of 1·6% of moisture by the reagents used. To test this hypothesis, three parallel experiments were conducted.

(1) The oxychloride (3·84 g., 1 mol.) was added quickly to pyridine (3·95 g., 2 mols.) in dry ether (40 c.c.) at 0°. A small amount of white solid (0·318 g.) (Found: Cl, 20·16; P, 6·0; C_5H_5N, 65·0%) separated at once, and no further change took place during 48 hrs. at 15°.

(2) With the same quantities, but with water (0·45 g.) added to the ethereal solution of pyridine, an oil which crystallised as described by Boyd and Ladhams was produced on the addition of the oxychloride. The ethereal solution was decanted, the solid rapidly washed with dry ether, and placed in a vacuum desiccator for 2 hours (4·42 g.) (Found: Cl, 22·6; P, 7·0; C_5H_5N, 53·2%).

(3) When atmospheric moisture was allowed to enter the reaction flask containing the dry reagents, by occasional removal of the stopper, the resulting solid had the composition Cl, 22·4; P, 9·8; C_5H_5N, 54·5 (Calc. for $POCl_2{\cdot}OH,2C_5H_5N$: Cl, 24·2; P, 10·6; C_5H_5N, 53·9%).

Interaction of Tri-β-octyl Phosphate and Phosphorus Oxychloride.—The following experiments were conducted with specimens of the ester (4·34 g., 1 mol.) prepared as described in the foregoing.

(1) There was no heat effect when the oxychloride (6·0 g., 4 mols.) was added at 15°. After 48 hours at 15°, then 48 hours at 15 mm. in a desiccator containing solid sodium hydroxide, the product (6·4 g. Calc. for dichlorophosphate, $POCl_2{\cdot}OR$: 7·4 g.) (Found: Cl, readily hydrolysed, 22·3; P, 15·1. Calc. for $POCl_2{\cdot}OR$: Cl, 28·7; P, 12·55%) was given aqueous treatment, and β-octyl chloride (0·4 g.), a residue (0·5 g.), and from the carbonate solution, a residue (1·3 g.) (Found: P, 13·1%), were obtained.

(2) With the oxychloride (2 mols.) and the mixture at 15° for 60 hours, aqueous treatment then yielded β-octyl chloride (0·48 g.), a residue (1·21 g.) (Found: P, 10·2%), and from the carbonate solution, a residue (1·32 g.) (Found: P, 14·2%). These results show the presence of the chlorophosphates in the reaction mixture.

(3) With the oxychloride (0·5 mols.), and the mixture at 15° for 48 hours at 15 mm. over solid sodium hydroxide for 24 hours, the product was *di-β-octyloxyphosphoryl chloride* (5·1 g.) (Found: Cl, 10·7; P, 9·8. $C_{16}H_{34}O_3Cl_2P$ requires Cl, 10·4; P, 9·2%); after aqueous treatment, this yielded no β-octyl chloride, but a residue (3·5 g.), $n_D^{16°}$ 1·4432 (Found: P, 9·6%), and from the carbonate solution, a residue (0·5 g.), $n_D^{18°}$ 1·4392 (Found: P, 12·1%). These results show that the primary product was essentially the monochlorophosphate and a little of the dichloro-ester.

The use of oxychloride (0·9 mol.), the mixture being kept at 15° for 60 hours, increased the proportion of the dichloro- at the expense of the monochloro-ester.

A mixture of the tri-ester (6·59 g. 1 mol.) and oxychloride (4·5 g., 1·5 mols.) was kept at 60° for 2·5 hours. 4 G. of this product, after aqueous treatment, yielded β-octyl chloride (0·3 g.) and a residue (1·0 g.) of phosphoric esters. 7·0 G. of the primary product were treated with pyridine (5 g.) at −10°. Precipitation of white solid was slow but became faster as the temperature rose to 15°. After 12 hours the colourless liquid was decanted, and the residue washed with dry ether, the washings being added to the decanted liquid for aqueous treatment. The solid weighed 4·00 g. (Found: Cl, 20·7; C_5H_5N, 48·0%). From the ethereal solution, (−)β-octyl chloride (1·55 g.), b. p. 68°/22 mm., $\alpha_D^{16°}$ −21·1°, and a residue (1·72 g.), $n_D^{18°}$ 1·4440, $\alpha_D^{16°}$ +14·1° (Found: P, 8·6%), were obtained, showing that both chlorophosphates were formed; but it was only the dichloro-ester which reacted with pyridine at room temperature.

When the tri-ester (2·8 g., 1 mol.) was kept for 2 days at 15° with only 0·5 mol. of the oxychloride and then heated with pyridine (1 mol.) for 1 hour at 100°, it yielded octylene (0·5 g.), (−)β-octyl chloride (1·3 g.), b. p. 68°/23 mm., $\alpha_D^{18°}$ −9·2°, and a residue (0·3 g.). Apparently the monochloro-ester, too, interacted with pyridine at 100°, a behaviour resembling that of di-*n*-butoxyphosphoryl chloride (Gerrard, *loc. cit.*).

Interaction of (−)Phenylmethylcarbinol and Phosphorus Oxychloride.—These reagents could be mixed slowly or rapidly at 0° without evolution of hydrogen chloride. Kept at 0°, the mixture remained clear and colourless, and the slow production of α-chloroethylbenzene was not accompanied by evolution of hydrogen chloride. If the mixture was allowed to warm to 15° there occurred, after 1—1·5 hours, a rapid separation into two layers, accompanied by coloration and heat evolution, but still without evolution of hydrogen chloride. The lower layer was soluble in water, with evolution of much heat; the upper layer was insoluble. In none of the experiments with this hydroxy-compound was there any indication of the formation of phosphoric esters; all the phosphorus in the system was found in the aqueous solution after the aqueous treatment.

With the (−)alcohol (3·05 g., 1 mol.) and the stated amounts of oxychloride the following experiments were conducted. (1) The alcohol ($\alpha_D^{18°}$ −18·8°) was quickly added to the oxychloride (1 mol.) at 0°, and after 5 minutes, the mixture on aqueous treatment yielded mainly unchanged alcohol.

(2) The mixture as in (1) was allowed to warm to 15°, and was given aqueous treatment after the separation into two layers; (+)α-chloroethylbenzene (1·15 g.), b. p. 78°/18 mm., $n_D^{19°}$ 1·5277, $\alpha_D^{18°}$ +3·6° (Found: Cl, 25·0. Calc.: Cl, 25·2%), and a very viscous residue (1·75 g.) were obtained. (3) When the mixture was kept at 0° for 9 hours, two layers were formed; after aqueous treatment (+)α-chloroethylbenzene (1·85 g.), b. p. 77°/16 mm., $\alpha_D^{18°}$ +14·1° (from alcohol of $\alpha_D^{18°}$ −42·0°) (Found: Cl, 24·95%), and a viscous residue (1·14 g.) were obtained. The latter did not contain phosphorus. (4) With the alcohol ($\alpha_D^{18°}$ −42·0°) and oxychloride (0·5 mol.) at 0° for 9 hours, there was no separation; (+)α-chloroethylbenzene (2·0 g.), $\alpha_D^{18°}$ +19·5° (Found: Cl, 25·1%), and a residue (1·20 g.) were obtained. (5) The alcohol ($\alpha_D^{18°}$ −25·6°) and oxychloride (2 mols.) at 0° for 5 hours yielded, after aqueous treatment, (+)α-chloroethyl-

benzene (2·5 g.), b. p. 86°/25 mm., $\alpha_D^{18°}$ +5·2° (Found : Cl, 25·1%) and a residue (0·5 g.). (6) With oxychloride (3 mols.) at 0° for 4 hours, (+)α-chloroethylbenzene (1·7 g.), $\alpha_D^{16°}$ +4·6°, and a residue (1·2 g.) were formed.

Interaction of (−)Phenylmethylcarbinol and Phosphorus Oxychloride in the Presence of Pyridine.—The oxychloride was added dropwise to an ethereal solution of the alcohol (4·1 g., 1 mol., $\alpha_D^{18°}$ −18·8°) and pyridine (2·7 g., 1 mol.) at 0°. The separation of a white solid began immediately, and after an hour at 15°, this was filtered off, washed with dry ether, and the ethereal solution given aqueous treatment. Yields of α-chloroethylbenzene, RCl, and the composition of the precipitates for different proportions of oxychloride are shown in the table.

	Ethereal solution.			White precipitate.			
$POCl_3$, mols.	RCl, %.	$\alpha_D^{18°}$.	Cl, %.	G.	Cl, %.	P, %.	C_5H_5N, %.
0·37	40	+27·8°	24·95	4·0	17·1	9·5	51·0
0·72	45	+22·0	25·0	5·6	21·1	10·9	47·7
1·00	57	+18·0	25·2	6·35	26·6	11·2	42·2

Addition of oxychloride (1·03 g., 0·33 mol.) to the alcohol (2·44 g., 1 mol.) and pyridine (1·58 g., 1 mol.) in ethereal solution at −12° caused a very slow deposition of solid : for times up to 30 minutes, the amount of solid was small, and the yield of chloride 5%. The precipitate contained phosphorus, and the ratio $Cl_3 : C_5H_5N$ was consistently about 1 : 2. After 3 hours at −12°, a 25% yield of chloride, $\alpha_D^{18°}$ +22·0°, was obtained. When the reagents (alcohol of $\alpha_D^{18°}$ −18·8°) were mixed rapidly in ethereal solution at 0°, and kept at this temperature for 2 hours before aqueous treatment, the results shown below were obtained : the composition of the precipitate is given in atomic or molecular proportions.

					Proportions in precipitate.		
$POCl_3$, mols.	C_5H_5N, mols.	RCl, yield %.	Cl, %.	$\alpha_D^{18°}$.	Cl.	C_5H_5N.	P.
0·67	1	30	25·0	+27·5°	2·17	2·05	1
0·67	2	30	25·1	+35·5	2·1	2·4	1
1·0	2	47	25·3	+17·3	2·25	2·25	1

Finally, two experiments were conducted with the reagents mixed at 0° and then kept at 15° for 12 hours. The alcohol (3·66 g., α_D^{18} −25·6°, 1 mol.), the oxychloride (3·07 g., 0·67 mol.), and pyridine (4·8 g., 2 mols.) in ethereal solution formed a white precipitate (7·38 g.) (Found : Cl, 19·2; C_5H_5N, 46·3; P, 7·9%; $Cl : C_5H_5N : P = 2·07 : 2·23 : 1$), and (+)α-chloroethylbenzene (1·9 g., 45%), b. p. 78°/16 mm., $\alpha_D^{18°}$ +63·0°, $n_D^{20°}$ 1·5262 (Found : Cl, 24·9%). The aqueous washing of the decanted ethereal solution contained only traces of chloride and phosphate ions. In absence of ether, the alcohol (2·44 g., $\alpha_D^{18°}$ −42·1°, 1 mol.), oxychloride (2·03 g., 0·67 mol.), and pyridine (3·2 g., 2 mol.) yielded (+)α-chloroethylbenzene (1·9 g.), b. p. 80°/20 mm., $\alpha_D^{18°}$ +74·8°, $n_D^{18°}$ 1·5270 (Found : Cl, 25·0%).

In none of the experiments described was there the slightest indication of the formation of phosphoric esters : the phosphorus content of each precipitate and aqueous washings of the ethereal solution accounted for all the phosphorus in the system.

Interaction of Ethyl Mandelate and Phosphorus Oxychloride.—Mixtures of mandelate (3 g., 1 mol.) and oxychloride (3 g., 1·1 mols.) were allowed to stand for the time and at the temperature stated in the table, and were then given aqueous treatment. A distillate of unchanged mandelate and a highly viscous residue, which did not contain phosphoric esters, were obtained in each experiment. Carbonate solutions yielded residues (0·2 g.) which also were phosphoric ester-free. Very little hydrogen chloride was evolved in these experiments.

		Distillate, ROH, g.,				Distillate, ROH, g.,	
Temp.	Time, hrs.	b. p. 92—93°/3 mm.	Residue, g.	Temp.	Time, hrs.	b. p. 92—93°/3 mm.	Residue, g.
15°	2	2·7	0·1	60°	4	0·75	1·65
40—50	2	1·3	0·95	65	5	— ($POCl_3$, 2 mols.)	1·9
40—50	2·5	1·0	1·5				

Interaction of Ethyl (−)Mandelate and Phosphorus Oxychloride in Presence of Pyridine.—In ethereal solution, phosphorus oxychloride was added slowly to an ethereal solution of ethyl (−)mandelate (4·5 g., 1 mol., $\alpha_D^{18°}$ −130·1°) and pyridine (2 g., 1 mol.) at 0°. Precipitation of a white solid occurred immediately, but this was not simply pyridine hydrochloride, and some chloride, RCl, was formed at the same time. After 12 hours at 15° the solution was filtered and given aqueous treatment. Owing to the nearness of b. p.'s of ethyl mandelate and ethyl phenylchloroacetate, these were not separated ; the chlorine content indicates the amount of the latter present (Calc. : Cl, 17·9%).

The residues were highly viscous gums containing phosphoric esters. Speed of mixing has significance, and affects the composition of the precipitate within 2—3 units in the percentages in experiments with constant amounts of reagents. Oxychloride (0·33 mol.) will precipitate nearly all the pyridine in the system in time ; if, however, the rate of addition is such that the second third of a mol. is added before the first has completed its effect, the relative concentration of oxychloride is increased and this modifies the composition of the precipitate.

	Distillate, b. p.					Precipitate.			
$POCl_3$, mol.	92—93°/2—3 mm., g.	Cl, %.	$\alpha_D^{18°}$.	Residue, g.	P, %.	G.	Cl, %.	P, %.	C_5H_5N, %.
0·33	1·0	13·9	+ 53·1°	2·9	5·5	4·45	16·5	3·4	42·2
0·66	2·6	17·0	+102·3	1·0	—	4·30	23·7	10·2	46·0
1·0	2·1	12·1	+ 43·6	0·4	—	4·72	22·9	11·2	42·3

In absence of ether, the oxychloride was added to the mandelate (3·0 g., 1 mol., $\alpha_D^{18°}$ +44·0°) and pyridine at 0°. Precipitation of a solid began immediately. After 24 hours at room temperature, the mixture was given aqueous treatment.

$POCl_3$, mol.	C_5H_5N, mol.	Distillate, b. p. 92—93°/2—3 mm., g.	Cl, %.	$\alpha_D^{18°}$.	Residue, g.	P, %.
0·33	1	1·0	11·0	−12·4°	0·4° (0·65) *	4·2
0·66	1	2·0	14·6	−19·2	0·45	—
1·0	1	2·5	17·9	−31·2	0·2	—
1·0	2	1·5	6·8	−3·2	0·2	—

* From the carbonate solution.

The mandelate (3 g., 1 mol.) and oxychloride (5·12 g., 2 mols.) were mixed quickly at 15° (no evolution of heat), and then, after 4 hours at 65° and 1 hour at 65°/15 mm., the product was cooled to 0°, mixed with pyridine (2·62 g., 2 mols.), and the crystalline precipitate (3·332 g.) (Found: Cl, 21·6; P, 9·2; C_5H_5N, 42·5%) washed with dry ether. The residue from the ethereal solution did not yield any distillate, but left a dark red, highly viscous gum (1·8 g.).

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28. *The Composition of the Fat of the Puma or American Lion* (Felix concolor).

By FRANCISCO GIRAL.

The reserve fat of the carnivorous puma (or American lion) was found by ester-fractionation to contain the following acids: myristic 1·3, palmitic 22·4, stearic 26·9, arachidic 3·7, hexadecenoic 12·6, oleic 26·2, linoleic 2·3, and unsaturated C_{20}, 4·6% (wt.). It contained more stearic than palmitic acid, this being somewhat exceptional for an animal fat, other than in some instances of herbivorous animal and insect fats. The puma fat was also notable for its unusually high content of hexadecenoic acid, in comparison with the proportion (3—4%) of this acid which has been recorded in the reserve fats of almost all the larger mammals so far examined.

IT has been pointed out (Hilditch, "The Chemical Constitution of Natural Fats," London, 1940, p. 76) that the component acids of the fats of carnivorous animals have not been determined with any degree of precision. Partial analyses of a few fats are available, including those of the mink (Lode, *Fettchem. Umschau*, **1935**, **42**, 205) and of the American black bear (Hoyt, *Oil and Soap*, **1934**, **11**, 85; Rasmussen *et al.*, *ibid.*, **1943**, **20**, 159), and detailed accounts have now been given of the component acids of depot fats of the lion, cat, baboon, and some omnivorous or herbivorous wild animals (Hilditch and Sime, *Biochem. J.*, **1942**, **36**, 98) and of human body fats (Cramer and Brown, *J. Biol. Chem.*, **1943**, **151**, 427).

The present communication deals with the fat from an adult male puma, shot in August, **1943**, near Ozaluma, a village in the tropical region in the north of the state of Vera Cruz, Mexico. The natives render the fat from the subcutaneous and perinephric tissues of the puma, and attribute to it useful medicinal properties, especially for rheumatic conditions, but this appears unlikely to rest on any scientific basis. The animal feeds mainly on herbivorous mammals, especially species of deer and their young, and also on sheep and young horses.

EXPERIMENTAL.

The puma fat was a white solid with a slight yellow tinge, melted at 40—45°, and possessed the following analytical characteristics: saponification equivalent 324·7, iodine value 38·8, acid value 3·6, unsaponifiable matter 1·3%. The mixed fatty acids of the puma fat melted at 45—48°, and had mean molecular weight (equivalent) 278·7 and iodine value 46·7.

Determination of Component Acids.—The filtered fat (150 g.) was hydrolysed with alcoholic potassium hydroxide, and the resulting aqueous soap solutions were extracted continuously with ether for 30 hours in order to remove the unsaponifiable constituents. After the extracted aqueous solution had been acidified, the recovered mixed fatty acids were found to yield no acids volatile in steam, and were therefore submitted to separation of their lead salts from alcohol:

	G.	%	Mean *M*.	Iod. val.
"Solid" acids from insoluble lead salts	59·0	56·9	272·8	9·3
"Liquid" acids from soluble lead salts	44·7	43·1	275·3	99·7

The acids in each group were esterified with methanol in presence of sulphuric acid, and the methyl esters obtained, after removal of small proportions of unesterified acids, were distilled at 2 mm. pressure from a Willstätter bulb (Hilditch, *op. cit.*, pp. 367 *et seq.*). The characteristics of the ester-fractions obtained are in Table I.

TABLE I.

Fractionation of Methyl Esters from Puma Fat.

Esters of "solid" acids.					Esters of "liquid" acids.				
No.	G.	B. p.	Sap. equiv.	Iod. val.	No.	G.	B. p.	Sap. equiv.	Iod. val.
S 1	3·57	145—152°	268·3	2·0	L1	2·60	148—157°	262·3	67·9
S 2	4·03	152—154	270·3	3·8	L2	3·15	157—160	269·4	70·2
S 3	4·14	154—155	277·1	4·6	L3	4·53	160—164	278·7	89·7
S 4	5·08	155—156	280·3	5·4	L4	4·86	164—166	284·1	92·6
S 5	3·78	156—157	285·6	5·9	L5	5·38	166—167	289·4	91·2
S 6	3·31	157—158	287·5	6·3	L6	4·32	167	296·4	93·3
S 7	3·96	158—161	290·9	7·2	L7	3·18	167—168	300·0	97·5
S 8	2·45	161—163	294·2	7·9	L8	2·88	168—171	309·5	113·4
S 9	6·28	163—164	297·3	9·6	L9	2·35	Residue	315·7	120·2
S10	4·70	164—166	300·6	9·9					
S11	3·40	166—172	305·9	10·9		33·25			
S12	3·50	Residue	310·9	19·9					
	48·20								

Individual acids were identified as follows:

Palmitic acid (from fractions S3 and S4), recrystallised from alcohol, m. p. 60—61°, M.M.W. 261·2.
Stearic acid (from fractions S7, S8, and S9), recrystallised from alcohol, m. p. 68—69°, M.M.W. 282·3.
Arachidic acid (admixed with stearic, from fractions S11 and S12), recrystallised from alcohol, m. p. 71—72° M.M.W. 301·6.

The original puma fat in acetic acid solution gave no precipitate on addition of bromine, but in light petroleum solution gave a slight precipitate with bromine; these tests indicate the absence of linolenic and the presence of some linoleic acid in the fat.

The data in Table I. when calculated to mixtures of saturated, hexadecenoic, oleic, linoleic, and unsaturated acids of the C_{20} series, lead to the proportions of component acids given in Table II.

TABLE II.

Component Acids (% wt.) of Puma Fat.

	"Solid" acids (56·9%).	"Liquid" acids (43·1%).	Total acids, %.
Myristic	0·6	0·7	1·3
Palmitic	20·5	1·9	22·4
Stearic	26·9	—	26·9
Arachidic	3·7	—	3·7
Hexadecenoic	—	12·6	12·6
Oleic	5·2	21·0	26·2
Linoleic	—	2·3	2·3
Unsaturated C_{20}	—	4·6	4·6

DISCUSSION.

Although the chief component acids of the puma fat are palmitic, oleic, and stearic, the proportions of these exhibit certain differences from those observed in other animal depot fats, and in addition there is a larger proportion of hexadecenoic acid than is usual in this type of fat.

It is rather unusual to find more stearic than palmitic acid in an animal fat. It should be noted, however, that the proportion of palmitic acid is lower than in most animal fats, of which it usually forms 30 ± 3% of the total fatty acids (Hilditch, *op. cit.*, pp. 11, 80); on the other hand, the total amount of C_{16} acids (palmitic and hexadecenoic), 35·0%, is similar to that observed in the great majority of animal fats so far examined. The presence of more stearic than palmitic acid in a natural fat, although a characteristic feature of the seed fats of certain tropical families of plants, has only been noted in the animal kingdom in a few other instances:

	Palmitic, %.	Stearic, %.	
Indian goat	25·5	28·1	(Dhingra and Sharma, *J. Soc. Chem. Ind.*, 1938, **57**, 369).
South American sheep	21	30	(Armstrong and Allan, *ibid.*, 1924, **43**, 216T).
Australian sheep	25	31	(Collins *et al.*, *ibid.*, 1929, **48**, 46T).
Mylabris pustulata (insect)	13	32	(Iyer and Ayyar, *J. Indian Inst. Sci.*, 1931, **14A**, 40).
Melanopsus sp. (insect)	6·7	9·1	(Giral, unpublished observation).

The proportion of stearic acid in the puma fat, although large, does not exceed the limits of 28—30% which appears to be the maximum amount of this acid likely to occur in an animal depot fat (Hilditch and Murti, *Biochem. J.*, 1940, **34**, 1301). Nevertheless, the occurrence of over 20% of stearic acid in mammalian depot fats has hitherto been noted only in those of the herbivora (some of which are, incidentally, the chief food of the puma).

The unsaturated acids of puma fat are unusual only in their relatively high content of hexadecenoic acid (12·6%). This is as large as the proportion found in many marine animal oils, of which it is a characteristic, major component, and is larger than the amounts of this acid usually observed in the fats of birds or rats, other than those of rats fed on intensive carbohydrate or protein diets (Longenecker, *J. Biol. Chem.*, 1939, **128**, 645). The proportion of hexadecenoic acid in fats of the larger mammals, herbivorous or carnivorous is usually only 3—4%, but the fat of the Ceylon bear (Hilditch and Sime, *loc. cit.*) contains 11% of this acid, *i.e.*, approximately the same proportion as the puma fat now described. Apart from the comparatively low content of oleic acid, the remaining acids of the puma fat are, in kind and amount, similar to those of many other animals and call for no special comment.

Species, dietary and climatic conditions may all contribute to variations in the component acids of animal reserve fats, and it is not possible in the present instance to distinguish between the influence which any one or all of these factors may exert in the development of the two acids, stearic and hexadecenoic, which appear to be unusually prominent.

My thanks are due to Miss Sara Garcia Iglesias for supplying the specimen of puma fat, and to Miss Alicia Ayluard for her technical help with the experimental work.

LABORATORIOS "HORMONA" S.A., MEXICO D.F. [*Received, June 19th*, 1944.]

29. *Sulphanilamides of Some Aminopyrazoles, and a Note on the Application of* p-*Phthalimidobenzenesulphonyl Chloride to the Synthesis of Sulphanilamides.*

By M. J. S. Dewar and F. E. King.

By hydrolysis of their *p*-acetamidobenzenesulphonyl derivatives, sulphanilamides have been synthesised from 3-amino-, 4-amino-, 4-amino-3-methyl- and 5-amino-3-methyl-pyrazoles. p-*Phthalimidobenzenesulphonyl chloride* has been prepared in 95% yield and quantitatively converted into p-*phthalimidobenzenesulphonanilide*, but hydrolysis of the latter to the aminosulphonanilide occurs less readily than with the corresponding acetyl compound.

Biological tests of numerous sulphanilamides having established the superiority of those derived from nitrogenous heterocyclic compounds, several new aminosulphonamidopyrazoles have been prepared.

Each of the selected aminopyrazoles derives from ethyl 3-methylpyrazole-5-carboxylate (I), which has been synthesised by an improvement of Knorr's method (*Annalen*, 1894, **279**, 219) from ethyl acetylpyruvate and hydrazine. The methylpyrazole prepared from (I) by hydrolysis and decarboxylation was oxidised to pyrazole-3-carboxylic acid, and the aminopyrazole (Knorr, *Ber.*, 1904, **37**, 3520) obtained therefrom by the Curtius method was converted through the *p*-acetamidobenzenesulphonyl derivative into 3-*p*-aminobenzenesulphonamidopyrazole, described since this work was completed by Jensen (see *Chem. Abstr.*, 1942, 5793).

4-Aminopyrazole (Knorr, *loc. cit.*) was prepared from pyrazole—derived from the 3-carboxylic acid—by nitration and reduction of the 4-nitro-compound (Buchner and Fritzsch, *Annalen*, 1893, **278**, 265). Raney nickel hydrogenation has increased the yield of the base, which is 30—35% for chemical methods, to 88%. The recrystallised product of the action of *p*-acetamidobenzenesulphonyl chloride on the aminopyrazole was a *bisacetamidobenzenesulphonyl* derivative, but acid hydrolysis of the unpurified material gave a monosulphanilamide identical with the compound described by Raiziss, Clemence, and Freifelder (*J. Amer. Chem. Soc.*, 1941, **63**, 2739) as 4-*p*-aminobenzenesulphonamidopyrazole. The formation of a bisacetylsulphanilyl compound (cf. the corresponding disubstituted 3-aminopyrazole of Jensen, *loc. cit.*) suggests that the free sulphanilamide may be a derivative of the tautomeric imine, but the alkali-solubility of all our pyrazole sulphonamides excludes this possibility.

4-Nitro-3-methylpyrazole is also efficiently reduced over Raney nickel, the aminopyrazole being conveniently isolated as a *dihydrochloride*. The *p*-acetamidobenzenesulphonyl derivative was prepared in the usual way, and the p-*aminosulphonamide* liberated by acid hydrolysis.

5-Amino-3-methylpyrazole was prepared from the ester (I) by the Curtius reaction, and each intermediate in this degradation is described. Hydrolysis of the *p*-acetamidobenzenesulphonamide to 5-p-*aminobenzenesulphonamido-3-methylpyrazole* was effected in alkaline solution. The action of *p*-acetamidobenzenesulphonyl chloride on 3-methylpyrazole-5-carboxylic acid does not give a sulphanilamide but the *diketo-bis-3'-methylpyrazolopiperazine*.

The chlorosulphonation of phthalanil affords p-*phthalimidobenzenesulphonyl chloride* in nearly theoretical quantities. It is therefore more accessible than the corresponding acetyl compound, normally isolated in 60% yield, but in the phthalylsulphanilamides the protecting acyl group appears to be less easily removed. Thus, hydrolysis of the *phthalimidosulphonanilide* with sodium hydroxide is much slower than with the analogous acetyl compound, and the hydrazine method for the fission of phthalimido-groups (Ing and Manske, J., 1926, 2348) gave but little of the aminosulphonanilide. When the preparation of 1-*p*-aminobenzenesulphonamido-1 : 3 : 4-triazole was attempted from its *phthalyl* derivative, the more drastic conditions required totally destroyed the compound, whereas, the aminosulphonamide was obtained in 60% yield from the corresponding acetate. It is therefore concluded that the use of phthalimidobenzenesulphonyl chloride is unlikely to be advantageous except in the synthesis of sulphonamides of very stable amines. Four of the above sulphonamides were tested *in vitro* against *Streptococcus pyogenes*. Compared with sulphanilamide (equals 1), the 5-amino-3-methyl derivative has an activity of 3 : the index for 4-*p*-aminobenzenesulphonamidopyrazole is 1/3—1, and for 4-*p*-aminobenzenesulphonamido-3-methylpyrazole it is 1/9—1/3. The activity of 1-*p*-aminobenzenesulphonamido-1 : 3 : 4-triazole (sulphanilamide = 1) is 1/27—1/3.

Experimental.

Ethyl 3-Methylpyrazole-5-carboxylate.—Hydrazine hydrate (10 g., 0·2 mol.) in alcohol (25 c.c.) was added slowly with shaking and cooling to a solution of ethyl $\alpha\gamma$-diketo-*n*-valerate (31·6 g., 0·2 mol.) in alcohol (75 c.c.). After refluxing for 1 hour, the alcohol was distilled; the pyrazole (30·5 g., 99%) crystallised from aqueous alcohol in long acicular plates, m. p. 82° (Found : C, 54·7; H, 6·5. Calc. for $C_7H_{10}O_2N_2$: C, 54·5; H, 6·5%).

3-p-*Aminobenzenesulphonamidopyrazole.*—3-Aminopyrazole (5·8 g.) (Knorr, *loc. cit.*) and *p*-acetamidobenzenesulphonyl chloride (16·3 g.) in dry acetone (20 c.c.) and pyridine (8 c.c.) were left overnight at room temperature, and water then added. The gum which separated slowly solidified but could not be purified. Hydrolysis with acid proved unsatisfactory : the crude amide (5·6 g.) was therefore heated for 5 hours on a steam-bath with potassium hydroxide (3·4 g.) in water (10 c.c.); much tarry material was then removed by charcoal treatment, and the aminobenzenesulphonamide precipitated by acetic acid. Several crystallisations from water gave rhombic needles, m. p. 227—228°, easily soluble in alkali (Found : N, 23·7; S, 13·6. Calc. for $C_9H_{10}O_2N_4S$: N, 23·5; S, 13·4%). Jensen (*loc. cit.*) gives m. p. 235°.

4-p-*Aminobenzenesulphonamidopyrazole* (cf. Raiziss *et al.*, *loc. cit.*).—Catalytic reduction of 4-nitropyrazole (Buchner and Fritsch, *loc. cit.*) with Raney nickel gave the aminopyrazole, isolated as dihydrochloride, in 88% yield. Condensation of the hydrochloride (2·9 g.) with *p*-acetamidobenzenesulphonyl chloride (4·5 g.) in acetone (15 c.c.) and pyridine (5 c.c.) at room temperature gave, on pouring into water, a product from which, by repeated crystallisation from 50%

acetic acid, a ***bisacetamidobenzenesulphonamide*** was isolated in microscopic rhombs, m. p. 190—192° (Found : N, 14·2; S, 13·6. $C_{19}H_{19}O_6N_5S_2$ requires N, 14·7; S, 13·4%).

The crude acetyl compound (2·5 g.) was heated at 100° with hydrochloric acid (5 c.c., 20%) for 30 minutes, and the solution cooled, filtered from sulphanilic acid, and basified with ammonia. Crystallisation of the precipitated sulphonamide from water gave microscopic rhombs (1·07 g., 50%), m. p. 185° (Found : N, 23·5; S, 13·8. Calc. for $C_9H_{10}O_2N_4S$: N, 23·5; S, 13·4%).

4-Amino-3-methylpyrazole.—4-Nitro-3-methylpyrazole (6·7 g.), hydrogenated at 3 atms. in cold alcoholic solution (50 c.c.) with Raney nickel (2 g.), was reduced in 5 hours. The oily residue obtained by evaporation was dissolved in ether and precipitated by hydrogen chloride as the *dihydrochloride*, which crystallised from alcohol–ether in short hexagonal prisms (6·35 g., 89%), m. p. 195—200° (decomp.) (Found : N, 24·9; Cl, 40·9. $C_4H_9N_3,2HCl$ requires N, 24·7; Cl, 41·7%)

4-p-Aminobenzenesulphonamido-3-methylpyrazole.—The amine hydrochloride (3·18 g.) and *p*-acetamidobenzenesulphonyl chloride (4·6 g.) were left overnight with pyridine (5 c.c.) and acetone (15 c.c.). Addition of water gave the acetamidosulphonamide (4·17 g., 76%), which was heated at 100° for 30 minutes with hydrochloric acid (6 c.c., 20%). The *aminobenzenesulphonamide* precipitated from the cold filtered solution with ammonia crystallised from water in minute silvery plates (1·64 g., 61%), m. p. 176° (Found : N, 21·3; S, 12·4. $C_{10}H_{12}O_2N_4S$ requires N, 22·2; S, 12·7%).

3-Methylpyrazole-5-carbohydrazide.—Ethyl 3-methylpyrazole-5-carboxylate (58·4 g.) and hydrazine hydrate (25 g.), heated under reflux for 8 hours, gave a product which crystallised from water in stout hexagonal prisms containing water of crystallisation. After drying at 100°, the ***hydrazide*** (46·8 g., 90%) had m. p. 153—154° (Found : C, 42·9; H, 5·7. $C_5H_8ON_4$ requires C, 42·9; H, 5·7%).

3-Methylpyrazole-5-carbazidę.—To a solution of the hydrazide (46·8 g.) in 2N-nitric acid (250 c.c.), stirred and cooled below 5°, a solution of sodium nitrite (25 g.) in water (50 c.c.) was slowly added. After 1 hour, the *azide* was collected, washed with ice-water, and dried over calcium chloride in a vacuum (Found : N, 45·0. $C_5H_5ON_5$ requires N, 46·3%).

Ethyl 3-Methyl-5-pyrazylcarbamate.—The dry azide (41·9 g.) was refluxed in boiling alcohol (200 c.c.) for 5 hours; the solvent was then evaporated, and the residue dissolved in hot water. The ***urethane*** (25·6 g., 55%) separated in clusters of irregular plates, m. p., after falling to powder at 100°, 158—160° (Found : C, 49·7; H, 6·4; N, 25·1. $C_7H_{11}O_2N_3$ requires C, 49·7; H, 6·5; N, 24·9%). The urethane *picrate* crystallised from water in microscopic saffron rhombs, m. p. 148—150° (Found, after drying at 70°/0·01 mm. : N, 21·5. $C_7H_{11}O_2N_3,C_6H_3O_7N_3$ requires N, 21·1%). When the moist azide was used, ethyl 3-methylpyrazole-5-carboxylate was the reaction product.

5-Amino-3-methylpyrazole.—The urethane (25·5 g.) was heated with hydrated barium hydroxide (143 g.) in water (150 c.c.) under reflux for 3½ hours; the solution was then cooled, saturated with carbon dioxide, and filtered from barium salts. The filtrate was fractionated under reduced pressure, and the aminopyrazole (9·6 g., 65%) collected at 213°/14 mm. as a very viscous syrup which on keeping formed highly deliquescent crystals, m. p. 94°. The amine *picrate* crystallised from water in microscopic yellow needles, m. p. 205—209° (Found : N, 25·3. $C_4H_7N_3,C_6H_3O_7N_3$ requires N, 25·8%).

5-p-Aminobenzenesulphonamido-3-methylpyrazole.—*p*-Acetamidobenzenesulphonyl chloride (10·2 g.) was added to a solution of the amine (4·24 g.) in dry dioxan (30 c.c.) and pyridine (4·5 c.c.), which next day was diluted with water. The crude acetyl derivative (10·55 g., 81·5%) was collected, washed, and dried at 100°, and a portion (6·33 g.) heated for 3 hours on a steam-bath with potassium hydroxide (3·9 g.) in water (30 c.c.). Neutralisation with acetic acid precipitated the *aminobenzenesulphonamide* (2·7 g., 50%), which crystallied from aqueous alcohol in long needles, m. p. 253—254° (Found : N, 22·6; S, 13·2. $C_{10}H_{12}O_2N_4S$ requires N, 22·2; S, 12·7%).

2 : 5-Diketo-3 : 4 : 6 : 1-bis-(3′-methylpyrazolo)piperazine.—A pyridine solution of 3-methylpyrazole-5-carboxylic acid (1 mol.) and *p*-acetamidobenzenesulphonyl chloride (1 mol.) was heated for 30 minutes at 100° and then diluted with water. The precipitated solid, crystallised from acetic acid, yielded the *piperazine* as feathery masses of microscopic yellow rhombic plates decomposing above 270° (Found : C, 55·2; H, 3·7; N, 25·6. $C_{16}H_{14}O_2N_4$ requires C, 55·5; H, 3·7; N, 25·9%). The identical compound was also obtained from the pyrazolecarboxylic acid by the action of *p*-nitrobenzoyl chloride–pyridine.

p-Phthalimidobenzenesulphonyl Chloride.—Phthalanil (30 g.) was shaken and heated on a steam-bath with chlorosulphonic acid (30 c.c.) for 2 hours. When cool, the *sulphonyl chloride* (27·2 g., 95%) was isolated by pouring on ice, collected, and dried in a vacuum over sulphuric acid. Crystallisation from chlorobenzene gave acicular plates, m. p. 234—237° (Found : N, 4·6; Cl, 10·6. $C_{14}H_8O_4NClS$ requires N, 4·4; Cl, 11·0%).

p-Phthalimidobenzenesulphonanilide.—The phthalimidobenzenesulphonyl chloride (9·7 g.) and aniline (6·1 g.) were refluxed in acetone (30 c.c.) for 2 hours, and the *anilide* (11·5 g., 100%) isolated by addition of water. It crystallised from acetic acid in truncated hexagonal plates, m. p. 219—221° (Found : C, 62·9; H, 3·9; N, 7·3; S, 7·9. $C_{20}H_{14}O_4N_2S$ requires C, 63·5; H, 3·7; N, 7·4; S, 8·5%).

Hydrolysis of p-*Phthalimidobenzenesulphonanilide.*—Removal of the phthalyl group by heating the anilide (4·7 g.) on a steam-bath first with hydrazine hydrate (0·62 g.) in alcohol (20 c.c.) and then with hydrochloric acid (50 c.c. of 10%) gave, in small yield, *p*-aminobenzenesulphonanilide, m. p. 190—192°, not depressed by an authentic specimen.

The anilide (3·76 g., 0·01 mol.) was added to 2N-sodium hydroxide (50 c.c.) maintained at 100°, and at 15 minute intervals 5 c.c. portions were removed, added to 2N-hydrochloric acid (20 c.c.) and ice, and titrated with sodium nitrite solution (0·1022N) standardised against sulphanilic acid. A comparative experiment with *p*-acetamidobenzenesulphonanilide demonstrated the greater rate of hydrolysis of the latter.

p-Phthalimidobenzenesulphonanilide.				*p*-Acetamidobenzenesulphonanilide.	
Time (mins.).	Titre (c.c.).	Time (mins.).	Titre (c.c.).	Time (mins.).	Titre (c.c.).
15	1·8	90	6·8	15	7·5
30	3·2	105	7·3	30	8·5
45	4·5	120	7·7	45	8·8
60	5·5	600	9·3	300	8·8
75	6·2				

1-p-Phthalimidobenzenesulphonamido-1 : 3 : 4-triazole.—The aminotriazole (0·84 g.) (Ruhemann and Stapleton, J., 1899, **75**, 1132) and the phthalylsulphonyl chloride (3·4 g.) were heated at 100° in dioxan (25 c.c.) and pyridine (1 c.c.) for 2 hours, and the *sulphonamide* precipitated by addition of water. The product could not be crystallised and was therefore purified by treating its solution in alkali with charcoal, filtering and acidifying it (Found : S, 8·3. $C_{16}H_{11}O_4N_5S$ requires S, 8·7%). The compound was destroyed by all attempts to hydrolyse the phthalyl group.

1-p-Acetamidobenzenesulphonamido-1 : 3 : 4-triazole.—A mixture of 1-amino-1 : 3 : 4-triazole (4·08 g.) and *p*-acetamidobenzenesulphonyl chloride (11·4 g.) in dry dioxan (25 c.c.) and pyridine (5 c.c.), after standing overnight, deposited a gum which solidified when triturated with water. The *acetamidosulphonamide* (7·6 g., 59%) crystallised from water

in flat prisms, m. p. 205° (decomp.) (Found: S, 11·4. $C_{10}H_{11}O_3N_3S$ requires S, 11·4%). Hydrolysis at 100° with 20% hydrochloric acid gave the sulphanilamide (yield 60%) crystallising from water in needles, m. p. 225° (decomp.) (Found: C, 40·4; H, 4·0; S, 13·1. Calc. for $C_8H_9O_2N_3S$: C, 40·2; H, 3·8; S, 13·4%). Anderson, Faith, Marson, Winnek, and Roblin (*J. Amer. Chem. Soc.*, 1942, **64**, 2902) give m. p. 237° (corr.).

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DYSON PERRINS LABORATORY, OXFORD. [*Received, September 7th*, 1944].

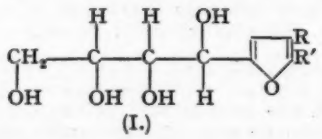
30. *The Condensation of Glucose and β-Diketones.*

By J. K. N. JONES.

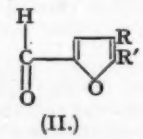
Glucose condenses with β-diketones in the presence of anhydrous zinc chloride to give derivatives of furan. These are converted into derivatives of pyran on heating with dilute aqueous acid. The ultra-violet absorption of several of these derivatives has been examined.

IN view of the publications of Müller and Varga (*Ber.*, 1939, **72**, 1993) and of Szeki and Laszlo (*Ber.*, 1940, **73**, 924) on the condensation products of glucose and β-diketones, it is opportune to summarise work in which the results of Szeki and Laszlo are confirmed and extended.

Glucose condenses with acetoacetic ester (West, *J. Biol. Chem.*, 1925, **66**, 63; Moore, Erlanger, and West, *ibid.*, 1936, **113**, 43), benzoylacetic ester, and acetonedicarboxylic ester (Szeki and Laszlo, *loc. cit.*) in the presence of anhydrous zinc chloride, with the formation of furan derivatives, (I; R = CO_2Et, R′ = Me, Ph, and $CH_2{\cdot}CO_2Et$ respectively). The constitution of these substances was proved by oxidation with lead tetra-acetate to the corresponding derivatives (II). Owing to war conditions, these publications were not available to the author, who had reached a similar conclusion from a study of the products of oxidation by periodic acid, of (I; R = CO_2Et, R′ = Me) and (I; R = COMe, R′ = Me), the latter having been prepared by condensation



(I.)



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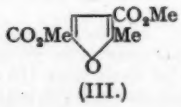
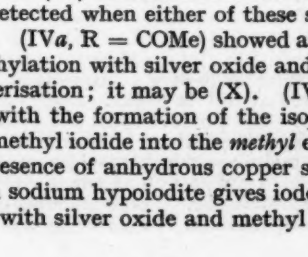


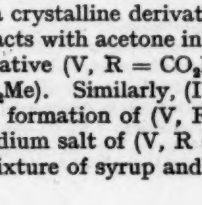
(III.)

of glucose and acetylacetone. These two compounds react quantitatively with 3 moles of periodic acid, with the formation of formaldehyde, formic acid, and the aldehydes (II; R = CO_2Et, R′ = Me and R = COMe, R′ = Me, respectively). The constitution of the aldehyde (II; R = CO_2H, R′ = Me) was proved by decarboxylating it to ω-methylfurfuraldehyde, identified as its oxime and 2 : 4-dinitrophenylhydrazone. Further proof was furnished by the isolation of the compound (III) after oxidative methylation of (I; R = CO_2H, R′ = Me) with silver oxide and methyl iodide. This showed an absorption band in water at 2620 A. The constitution of the new *substance* (I; R = COMe, R′ = Me) is inferred from its reactions, which are similar to those of (I; R = CO_2H, R′ = Me). The *aldehyde* (II; R = COMe, R′ = Me) showed an absorption band in water at 2850 A.

Substances (I; R = CO_2H, R′ = Me and R = COMe, R′ = Me) in boiling dilute acid solution rearrange with the elimination of the elements of water: substance (I, R = CO_2H) gives a pyran derivative (IV, R = CO_2H) (7 : 8-d-erythro-*dihydroxy*-2-*methyl*-1 : 5 : 6 : 7 : 8 : 9-*hexahydro*-1 : 5-*dioxanaphthalene*-3-*carboxylic acid*) and, by analogy, substance (I, R = COMe) is considered to give the pyran derivative (IV, R = COMe). Substances (IV, R = CO_2H and R = COMe) contain two alcoholic hydroxyl groups adjacent to each other, since

(IV.)

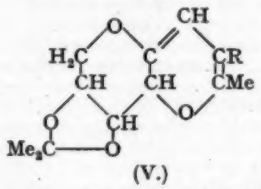


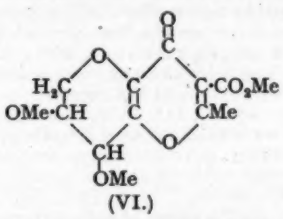


(IV*a*.)

they are oxidised by periodic acid with the formation of optically active dialdehydes (IV*a*) without loss of carbon atoms; one mole of (IV) consumes one mole of periodic acid. No selective absorption in the ultra-violet region could be detected when either of these substances (IV; R = CO_2H and R = COMe) was examined in aqueous solution. (IV*a*, R = COMe) showed an absorption band in water at 2700 A. (IV*a*, R = CO_2H) gave, on oxidative methylation with silver oxide and methyl iodide, a crystalline derivative in insufficient yield for complete characterisation; it may be (X). (IV, R = CO_2H) reacts with acetone in the presence of anhydrous copper sulphate with the formation of the iso*propylidene* derivative (V, R = CO_2H), which is converted by silver oxide and methyl iodide into the *methyl* ester (V, R = CO_2Me). Similarly, (IV, R = COMe) reacts with acetone in the presence of anhydrous copper sulphate with the formation of (V, R = COMe). Oxidation of this product with sodium hypoiodite gives iodoform and the sodium salt of (V, R = CO_2H). Methylation of (IV, R = CO_2H) with silver oxide and methyl iodide gives a mixture of syrup and crystals. This crystalline

product of unknown constitution shows no observable rotation in methyl alcohol and appears to be formed from (V, R = CO_2H) by oxidation and methylation, since it possesses an extra oxygen atom. A possible


(V.)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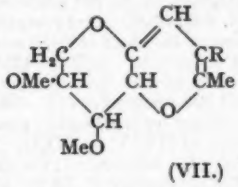
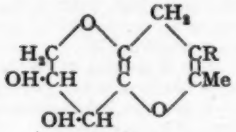
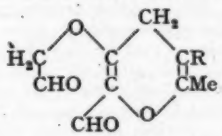
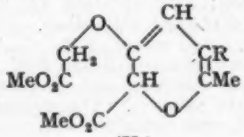

(VII.)

formula is (VI). The *dimethyl* derivative (VII) of (IV, R = CO_2H) is more readily prepared by methylation with caustic soda and methyl sulphate. The corresponding *methyl* ester (VII, R = CO_2Me) results on methylation of the acid with silver oxide and methyl iodide. Both the ester and the acid, on oxidation with nitric acid, give *meso*-dimethoxysuccinic acid, which is also similarly produced from (VI).

The possibility that substance (IV, R = CO_2H or COMe) may have structure (VIII) is excluded because oxidation of this with periodic acid would give an optically inactive derivative (IX). The hydroxyl groups which are free in (IV) must be on C_4 and C_5 of the original glucose unit, since they are adjacent (periodic acid


(VIII.)


(IX.)


(X.)

oxidation), an *iso*propylidene derivative is readily prepared, and *meso*-dimethoxysuccinic acid is isolated after oxidation of (VII) with nitric acid.

Experimental.

Oxidation of 2-Methyl-5-(d-arabo-tetrahydroxybutyl)furan-3-carboxylic Acid (I; R = CO_2H, R′ = Me).—The acid (217 mg.) was oxidised with aqueous periodic acid at 30°; it reduced 32·2 c.c. of 0·1N-periodic acid in 10 mins. (constant value) (Found: equiv., 42·4. Calc. for $C_{10}H_{14}O_7$: equiv., 40·6, on the assumption that three atoms of oxygen are consumed per mole of the carboxylic acid).

During the oxidation crystals of the aldehyde (II; R = CO_2H) separated; they were recrystallised from acetone and water. The product, 5-formyl-2-methylfuran-3-carboxylic acid (70 mg.), m. p. 176°, $[\alpha]_D^{20°}$ 0° (in acetone; *c*, 1·2), gave no colour with aqueous ferric chloride (Found: C, 54·4; H, 4·6; equiv., 157. Calc. for $C_7H_6O_4$: C, 54·6; H, 3·9%; equiv., 154).

Decarboxylation of the Aldehyde (II; R = CO_2H, R′ = Me).—The aldehyde (1 g.) was dissolved in quinoline (25 c.c.), copper chromite (0·2 g.) added, and the solution boiled for 4 hrs. (evolution of carbon dioxide). The cooled solution was poured into water and extracted with ether (twice), and the combined extracts shaken successively with 2N-hydrochloric acid (twice), sodium carbonate solution, and water. The ethereal extract was dried (anhydrous sodium sulphate) and evaporated to a syrup (0·6 g.). This syrup with hydroxylamine gave the oxime of ω-methylfurfuraldehyde, identical with the oxime prepared from ω-methylfurfuraldehyde obtained from rhamnose. The oxime was isolated in its two forms, m. p. 110° and m. p. 50°. The 2 : 4-dinitrophenylhydrazone of the aldehyde also was obtained in two forms, a red form, m. p. and mixed m. p. with a synthetic specimen 173°, and a purple-black form which was not obtained pure.

Oxidation of the Ethyl Ester (I; R = CO_2Et, R′ = Me).—The ester (97 mg.) at 20° reduced 20·5 c.c. of 0·1N-periodic acid in 15 mins. (constant value) (Found: equiv., 47·3. Calc. for $C_{12}H_{18}O_7$: equiv., 45·7) (assuming three atoms of oxygen are consumed). During the reaction the crystalline ethyl ester (II, R = CO_2Et) separated, m. p. 59° after recrystallisation from ether–light petroleum (b. p. 40—60°). With dinitrophenylhydrazine hydrochloride solution this gave the red *dinitrophenylhydrazone*, m. p. 234° (decomp.) after recrystallisation from dioxan (Found: C, 49·6; H, 3·97; N, 15·85. $C_{18}H_{14}O_7N_4$ requires C, 49·7; H, 3·9; N, 15·5%).

From the dioxan mother-liquor a small quantity of formaldehyde-2 : 4-dinitrophenylhydrazone was obtained, m. p. (after recrystallisation from methyl alcohol) and mixed m. p. with an authentic sample 165°.

Methylation of 2-Methyl-5-(d-arabo-tetrahydroxybutyl)furan-3-carboxylic Acid.—The acid (0·7 g.), dissolved in acetone, was methylated with silver oxide and methyl iodide. After the initial vigorous reaction had subsided, the mixture was refluxed for 6 hrs. and then worked up in the usual manner. The syrup (0·6 g.) was distilled in a vacuum and gave a small quantity of crystals mixed with syrup [b. p. 100°/0·1 mm. (bath temp.)]. The crystals (III) were collected on a tile and recrystallised from light petroleum (b. p. 40—60°); m. p. 53°, $[\alpha]_D^{20°}$ ±0° (*c*, 1·79 in methyl alcohol) (Found: C, 54·5; H, 5·5; OMe, 31·4; equiv., 98. Calc. for $C_9H_{10}O_5$: C, 54·6; H, 5·1; OMe, 31·3%; equiv., 99).

Acidification of the solution used for the determination of the equivalent weight gave, after extraction with ether, the free acid, m. p. 270° (decomp.) after recrystallisation from ethyl acetate (Found: C, 49·4; H, 3·7; equiv., 85. Calc. for $C_7H_6O_5$: C, 49·4; H, 3·5%; equiv., 85).

7 : 8-d-erythro-Dihydroxy-2-methyl-1 : 5 : 6 : 7 : 8 : 9-hexahydro-1 : 5-dioxanaphthalene-3-carboxylic Acid (IV, R = CO_2H).—(*a*) The acid (I, R = CO_2H) (10 g.) was dissolved in water (100 c.c.) and boiled under reflux: $[\alpha]_D^{20°}$ −17° (initial value); −34° (½ hr.); −57° (1 hr.); −67° (1½ hrs.); −72° (2 hrs.); −74° (2½ hrs.); −74° (3 hrs.). The solution was then cooled and evaporated, under reduced pressure; the crystals which separated were recrystallised from the minimum quantity of hot water or from ethyl acetate. Yield 6 g., m. p. 142° (Found: equiv., 233. Calc. for $C_{10}H_{12}O_6$: equiv., 228).

(*b*) The acid (I, R = CO_2H) (1 g.) was heated at 170° for 5 mins. and then cooled to 20°. Water and gas were evolved during the heating. Recrystallisation of the residue from ethyl acetate gave (IV, R = CO_2H) in 54% yield, m. p. and mixed m. p. 142°.

isoPropylidene Derivative (V, R = CO_2H).—The acid (IV, R = CO_2H) (5 g.) was shaken with dry acetone (100 c.c.) and anhydrous copper sulphate (25 g.) for 24 hrs. The filtered solution was evaporated under reduced pressure at 30°,

and the crystalline residue (5·5 g.) recrystallised from benzene–light petroleum (b. p. 40—60°). Yield 5·2 g., m. p. 118°, $[\alpha]_D^{20°}$ −95° (*c*, 0·52 in ethyl alcohol) (Found: C, 58·3; H, 6·5; equiv., 274. $C_{13}H_{16}O_8$ requires C, 58·2; H, 6·0%; equiv., 268).

Methylation of this product with silver oxide and methyl iodide gave quantitatively the corresponding *methyl* ester (V, R = CO_2Me), m. p. 99° after recrystallisation from absolute alcohol, $[\alpha]_D^{20°}$ −89° (*c*, 1·5 in absolute alcohol) (Found: C, 59·6; H, 6·0; OMe, 11·6; equiv., 279. $C_{14}H_{18}O_8$ requires C, 59·6; H, 6·4; OMe, 11·0%; equiv., 282).

Oxidation of the Acid (IV, R = CO_2H).—The acid (113 mg.) was oxidised with aqueous periodic acid, and the change of rotation followed: $[\alpha]_D^{20°}$ −120° (initial value); −31° (4 mins.); −23° (25 mins., constant value). The solution reduced 9·8 c.c. of 0·1N-periodic acid [Found: equiv., 115. Calc. for $C_{10}H_{12}O_6$: equiv., 113, assuming one oxygen atom is consumed per mole of (IV)]. No crystals separated and no formaldehyde could be detected in the solution. Dinitrophenylhydrazine hydrochloride solution, however, gave an orange precipitate which could not be obtained crystalline.

Oxidation of (IV, R = CO_2H) (755 mg.) with periodic acid in concentrated aqueous solution (5 c.c.) at 0° caused the precipitation of a *substance* (IV*a*, R = CO_2H) (540 mg.), m. p. 146°, $[\alpha]_D^{20°}$ −25° (*c*, 0·44 in water) (Found: C, 53·3; H, 4·6. $C_{10}H_{10}O_6$ requires C, 53·2; H, 4·5%). Methylation of this material (50 mg.) with silver oxide and methyl iodide in the usual manner gave a crystalline *substance* [X (?), R = CO_2Me] (14 mg.), m. p. 119° after recrystallisation from methyl alcohol (Found: OMe, 31·3. $C_{13}H_{16}O_8$ requires OMe, 31·0%).

Methylation of the Acid (IV, R = CO_2H).—(a) *With silver oxide and methyl iodide.* The acid (2 g.), dissolved in methyl alcohol, was methylated with silver oxide and methyl iodide; after the initial reaction had subsided, the mixture was refluxed for 6 hrs. and then worked up in the usual manner. The resultant syrup (2·1 g.), $n_D^{17°}$ 1·4978, was distilled in a vacuum and the following fractions obtained: 1 g., b. p. 140°/0·1 mm. (bath temp.), $n_D^{18°}$ 1·4938; 0·4 g., b. p. 150°/0·1 mm. (bath temp.), $n_D^{17°}$ 1·4926; 0·2 g., b. p. 160°/0·1 mm. (bath temp.), $n_D^{17°}$ 1·4918.

The first fraction partly crystallised. The crystals [VI (?)] were collected on a tile and recrystallised from methyl alcohol; m. p. 126°, $[\alpha]_D^{20°}$ ±0° (*c*, 1·0 in methyl alcohol) (Found: C, 54·6; H, 6·3; OMe, 32·5; equiv., 244. $C_{12}H_{16}O_7$ requires C, 54·6; H, 6·3; OMe, 32·5%; equiv., 286). After determination of the equivalent weight the solution was acidified and extracted with ether. Concentration of the extracts gave a crystalline *acid*, m. p. 151° (Found: C, 52·9; H, 5·7; OMe, 23·4; equiv., 278. $C_{12}H_{16}O_7$ requires C, 52·9; H, 5·9; OMe, 22·8%; equiv., 272).

(b) *With methyl sulphate and 30% sodium hydroxide solution.* The acid (10 g.) was dissolved in water (10 c.c.) and acetone (10 c.c.) and methylated at 30° by the gradual addition (1 hr.) of sodium hydroxide solution (30%, 200 c.c.) and methyl sulphate (95 c.c.). The mixture was stirred for 3 hrs., heated at 60° for 15 mins., cooled, acidified with dilute sulphuric acid, and extracted with ether (50 c.c.) (twice) and then with chloroform (50 c.c.) (twice). The combined extracts were washed with water, dried (anhydrous sodium sulphate), and evaporated under reduced pressure at 40° to a syrup (10 g.). The syrup was dissolved in methyl iodide (30 c.c.), and silver oxide added. The reaction was moderated by cooling, and the mixture then kept at 20° for 48 hrs. The product was worked up in the usual manner, and the resultant syrup (VII, R = CO_2Me) (10 g.), $n_D^{19°}$ 1·4972, was distilled under reduced pressure; b. p. 140° (bath temp.)/0·01 mm., $n_D^{20°}$ 1·4973, $[\alpha]_D^{20°}$ −105° (*c*, 2·6 in methyl alcohol) (Found: C, 57·6; H, 6·9; OMe, 33·6; equiv., 273. $C_{13}H_{18}O_8$ requires C, 57·8; H, 6·7; OMe, 34·4%; equiv., 270).

This material (7·5 g.) was heated with N-sodium hydroxide (30 c.c.) on the boiling water-bath for 6 hrs., and N-sulphuric acid (30 c.c.) then added to the cooled solution. The light brown oil which separated was extracted with ether, and the extract dried over anhydrous sodium sulphate. Solvent was removed in a vacuum, and the residual *acid* (VII, R = CO_2H) distilled; b. p. 180° (bath temp.)/0·01 mm., $n_D^{20°}$ 1·5130, $[\alpha]_D^{20°}$ −97° (*c*, 1·8 in methyl alcohol) (Found: C, 56·0; H, 6·4; OMe, 23·0; equiv., 254. $C_{12}H_{16}O_8$ requires C, 56·1; H, 6·3; OMe, 24·2%; equiv., 256). The acid formed in concentrated hydrochloric acid a deep blue solution, the colour of which was destroyed on heating with the separation of a brown oil.

This syrup (2·3 g.) was oxidised with nitric acid (*d* 1·42) (10 c.c.), and the solution worked up as described below. From the residual syrup a product (0·6 g.), b.p. 90° (bath temp.)/0·01 mm., $n_D^{20°}$ 1·4462, was obtained by fractional distillation. This crystallised on standing and, after trituration with ether–light petroleum (b. p. 40—60°), the methyl ester of *meso*-dimethoxysuccinic acid was isolated, m. p. 67° not depressed by an authentic specimen. With methyl-alcoholic ammonia this gave *meso*-dimethoxysuccinamide, m. p. and mixed m. p. with an authentic specimen, 244°.

Oxidation of the Crystalline Methylated Derivative [VI (?)].—The crystals (200 mg.) were oxidised with nitric acid (*d* 1·42) (2 c.c.) at room temperature and then at 70—80°, the reaction being moderated by cooling. After standing at 20° for 12 hrs., the solution was concentrated under reduced pressure, and methyl alcohol distilled through the residue to remove nitric acid and water. The residual syrup was esterified with methyl-alcoholic hydrogen chloride, and the mixed neutral esters isolated after neutralisation with silver carbonate. Fractional distillation of the syrup in a vacuum gave the dimethyl ester of *meso*-dimethoxysuccinic acid (20 mg.), m. p. and mixed m. p. with an authentic specimen, 66—67°.

Condensation of Glucose and Acetylacetone. Preparation of 2-Methyl-5-(d-arabo-tetrahydroxybutyl)-3-furyl Methyl Ketone (I; R = COMe, R′ = Me).—Glucose (25 g.) was heated with acetylacetone (12 g.) in methyl alcohol (12 c.c.) and anhydrous zinc chloride (12 g.) on the boiling water-bath until a clear solution was obtained (30 mins.). The solution was poured into water, and the precipitated crystals (3 g.) collected after 12 hrs. The *product* (I; R = COMe, R′ = Me) was recrystallised from hot methyl alcohol; m. p. 152°, $[\alpha]_D^{20°}$ −18° in water (*c*, 5·0) (Found: C, 54·1; H, 6·8. $C_{11}H_{16}O_8$ requires C, 54·1; H, 6·6%). With dinitrophenylhydrazine hydrochloride solution it gave a scarlet *derivative*, m. p. 142° (Found: C, 48·2; H, 4·8; N, 14·3. $C_{17}H_{20}O_9N_4$ requires C, 48·1; H, 4·7; N, 13·2%).

The substance (122 mg.) reduced 0·1N-periodic acid (30 c.c.), whence the equivalent weight is 40·7 (calc., 40·6 on the assumption that 1 mole reduces 3 moles of periodic acid). During the reaction crystalline *5-formyl-2-methyl-3-furyl methyl ketone* (II; R = COMe, R′ = Me) separated, m. p. 104—105° after recrystallisation from acetone and water (Found: C, 63·2; H, 5·2. $C_8H_8O_3$ requires C, 63·2; H, 5·3%). This gave an orange *dinitrophenylhydrazone*, m. p. 202° after recrystallisation from dioxan (Found: C, 49·2; H, 3·9; N, 17·9. $C_{14}H_{12}O_6N_4$ requires C, 49·1; H, 3·5; N, 16·4%).

7:8-d-erythro-Dihydroxy-2-methyl-1:5:6:7:8:9-hexahydro-1:5-dioxa-3-naphthyl Methyl Ketone (IV, R = COMe). —(I; R = COMe, R′ = Me) (2·5 g.) was boiled with 10% aqueous acetic acid (50 c.c.), and the change of rotation observed: $[\alpha]_D^{20}$ −17·6° (initial); −58° (¼ hr.); −81° (1 hr.); −91° (2½ hrs.); −94° (3 hrs.; constant value). The solution was then concentrated under reduced pressure, and the residual crystals (IV, R = COMe) recrystallised from acetone–light petroleum (b. p. 40—60°). Yield 2·2 g., m. p. 102°, $[\alpha]_D^{20°}$ −104° (*c*, 0·41 in methyl alcohol) (Found: C, 58·2; H, 6·2. $C_{11}H_{14}O_5$ requires C, 58·4; H, 6·2%). This *substance* gave neither crystalline oxime nor dinitrophenylhydrazone.

Substance (IV, R = COMe) was readily oxidised with periodic acid, 1 mole reducing 1 mole of the acid to iodic acid. During the reaction a *product*, m. p. 128—129° (*ex* acetone–light petroleum, b. p. 40—60°) separated, $[\alpha]_D^{20°}$ −23° (*c*, 0·2 in methyl alcohol) (Found: C, 54·6; H, 5·6. $C_{11}H_{12}O_5,H_2O$ requires C, 54·5; H, 5·8%).

Preparation of the iso*Propylidene Derivative* (V, R = COMe).—A solution of (IV, R = COMe) (1 g.) in acetone (20 c.c.) was shaken with anhydrous copper sulphate (10 g.) for 24 hrs., filtered, and concentrated under reduced pressure. The

residual crystalline solid (1 g.), recrystallised from aqueous methyl alcohol, had m. p. 96° (Found: C, 63·4; H, 7·3. $C_{14}H_{18}O_8$ requires C, 63·2; H, 6·9%).

This *product* (129 mg.) was dissolved in methyl alcohol (10 c.c.) and oxidised with an excess of 0·1N-iodine (50 c.c.) in 2N-sodium hydroxide (30 c.c.). After standing for 30 mins. at 20°, the precipitated iodoform was collected (141 mg.; 80%). The filtrate was acidified with dilute sulphuric acid, the excess of iodine removed with sulphur dioxide, and the solution extracted with ether (20 c.c. portions; thrice). The extracts were dried (anhydrous sodium sulphate) and evaporated to dryness. The crystalline residue (110 mg.), recrystallised from ether–light petroleum (b. p. 40—60°), had m. p. and mixed m. p. with an authentic specimen of the acid (V, R = CO_2H), 118°.

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31. *Carbohydrate Sulphuric Esters. Part III. The Hydrolysis of* iso*Propylidene Glucofuranose Sulphates and Methylglucofuranoside Sulphates.*

By E. G. V. PERCIVAL.

The alkaline hydrolysis of the barium salts of 1 : 2-monoacetone glucofuranose-6-sulphate (I), 1 : 2-monoacetone glucofuranose-3-sulphate (II), diacetone glucofuranose-3-sulphate (III), *methylglucofuranoside-6-sulphates* (IV) and *methylglucofuranoside-3-sulphates* (V) has been studied. The sulphate residue of (I) was rapidly eliminated with the production of 1 : 2-monoacetone 3 : 6-anhydroglucofuranose (VI) and 1 : 2-monoacetone glucofuranose (VII), whereas (II) was hydrolysed very slowly to give (VII) only, the rate of hydrolysis being approximately identical with that of (III). The sulphate residues on (IV) and (V) were readily removed and derivatives of 3 : 6-anhydroglucose (VIII) and of glucose (IX) were isolated in both cases.

The conclusion is reached that for sulphates, as distinct from toluene-*p*-sulphonates, ethylene oxide rings are not formed on treatment with alkali, whereas 3 : 6-anhydro-rings are formed [except for (II)]. The significance of these results in connection with the carragheen polysaccharide is discussed.

IN our studies on carragheen moss (Buchanan, Percival, and Percival, J., 1943, 51) we assumed that the hydrolysis of sulphuric ester residues would follow a course similar to that of toluene-*p*-sulphonic esters in the sugar group. The sole experimental evidence for this assumption was the isolation of 3 : 6-anhydromethylhexosides from the products of the alkaline hydrolysis of methylglycopyranoside sulphates (Part II, J., 1941, 830). No information was available, however, as to whether the hydrolysis of a carbohydrate sulphate with a suitably placed hydroxyl group would follow the course, familiar for the toluene-*p*-sulphonates, of ethylene oxide ring formation with the accompanying Walden inversion, or not. Owing to the insolubility in non-aqueous solvents of the salts of carbohydrate sulphates, it is not at present feasible to answer this question directly by the isolation of a product containing such a ring system, on treatment with sodium methoxide; but reliance may be placed on an analysis of the products of complete hydrolysis with alkali, since the ethylene oxide ring compounds, if formed, should be decomposed in two ways with the concomitant inversions on both carbon atoms concerned (Peat, *Ann. Reports*, 1939, 258).

From the experiments described below, it appears that ethylene oxide rings are not formed on the alkaline hydrolysis of sulphates, but that in most cases 3 : 6-anhydro-ring formation together with removal of the sulphate group, without inversion, take place.

Ohle and von Vargha (*Ber.*, 1928, **61**, 1203; 1929, **62**, 2435) showed that treatment of 1 : 2-monoacetone glucofuranose-6-toluene-*p*-sulphonate with sodium methoxide gave 1 : 2-monoacetone 5 : 6-anhydroglucose, which on hydrolysis with aqueous alkali yielded 1 : 2-monoacetone glucofuranose (VII) and 1 : 2-monoacetone *l*-idofuranose. As pointed out by Peat (*loc. cit.*), this indicates a preferential formation of the 5 : 6- as against the 3 : 6-anhydride, for 3 : 6-anhydride formation takes place only when the hydroxyl group on C_5 is substituted as in the conversion of 1 : 2-monacetone 5 : 6-ditoluene-*p*-sulphonyl glucose into 1 : 2-monoacetone 3 : 6-anhydro-5-toluene-*p*-sulphonyl glucose by Ohle, von Vargha, and Erlbach (*Ber.*, 1928, **61**, 1211). When, however, barium 1 : 2-monoacetone glucofuranose-6-sulphate (I) was treated with alkali, almost equal amounts of 1 : 2-monoacetone 3 : 6-anhydroglucofuranose (VI) and 1 : 2-monoacetone glucofuranose (VII) were obtained and no *l*-idose derivatives could be detected; here, therefore, we have evidence of the preferential formation of a 3 : 6- as against a 5 : 6-anhydride, contrary to the case of the toluene-*p*-sulphonate.

This observation led to a study of the hydrolysis of barium 1 : 2-monoacetone glucofuranose-3-sulphate (II), but this compound proved to be remarkably resistant to hydrolysis (Table I), in sharp contrast to the

TABLE I.

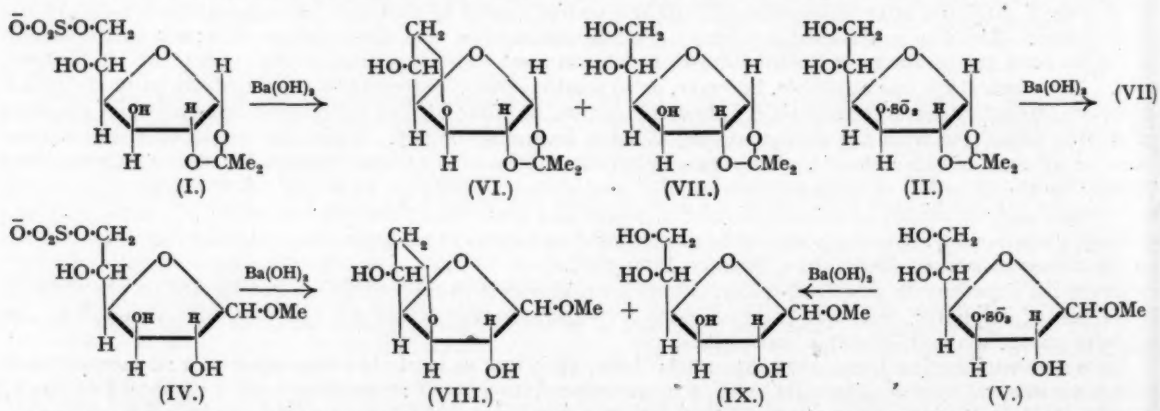
	Time (hours).	% Hydrolysis (mean) in 2·83N-NaOH at 100°.		Time (hours).	% Hydrolysis (mean) in 2·83N-NaOH at 100°.
Barium monoacetone glucose-6-sulphate	0·75	83	Barium methylglucofuranoside-6-sulphates	0·5	55
	1·5	85		1·5	76
	3·5	92		2·5	86
Barium monoacetone glucose-3-sulphate	16	3	Barium methylglucofuranoside-3-sulphates	0·82	55
	47	12		1·5	76
	54	10		3·75	87
Barium diacetone glucose-3-sulphate	15	2			
	47	12·5			

corresponding 6-sulphate, and 1 : 2-monoacetone glucofuranose (VII) was the only product isolated. Apart from the difficulty of hydrolysis this is parallel to the behaviour of the corresponding toluene-*p*-sulphonate, for von Vargha (*Ber.*, 1936, **69**, 2098) obtained 1 : 2-monoacetone glucose quantitatively on hydrolysis of this compound at 100° for 5 hours in aqueous-alcoholic sodium hydroxide (1·25N). Barium diacetone glucofuranose-3-sulphate (III) underwent hydrolysis at the same rate as the monoacetone derivative (cf. Part I, J., 1940, 1475, for the hydrolysis of barium diacetone galactopyranose-6-sulphate), a fact which supports the view that there is no interaction between the sulphate group on C_3 and the hydroxyl group on C_6 when 1 : 2-monoacetone glucofuranose-3-sulphate is treated with alkali.

These results appear to show that 3 : 6-anhydride formation cannot take place when the hydroxyl group on C_3 is esterified when a furanose ring is present. The behaviour of barium 1 : 2-monoacetone glucofuranose-3-sulphate (II) appears to be anomalous, however, since the corresponding derivative of the methylglucofuranosides (V) readily released the sulphate group on treatment with alkali and the products of hydrolysis clearly contained 3 : 6-anhydromethylglucofuranosides (VIII) and methylglucofuranosides (IX), since on suitable treatment 3 : 6-anhydroglucosazone and 3 : 6-anhydrogluconamide, together with the corresponding glucose derivatives, were isolated. Whether the stability of (II) is due to the fact that both the hydroxyl groups on C_2 and C_4 are occupied or is a consequence of the *iso*propylidene bridge between C_1 and C_2 must be left for further investigation.

The alkaline hydrolysis of the barium methylglucofuranoside-6-sulphates (IV) followed a similar course to that of (V), both in speed and in the products formed.

The yield of glucosazone (*ca.* 50%) and 3 : 6-anhydroglucosazone (*ca.* 20%) of the total amount of crude osazone obtained in both cases made necessary a careful search for other hexosazones, to determine whether ethylene oxide ring formation had played a part in the elimination of the sulphate residues. The barium methylglucofuranoside-6-sulphates (IV) would have been expected to yield the corresponding 5 : 6-anhydride, which should have given eventually glucosazone and *l*-sorbosazone (from *l*-idose) in about equal quantities (Ohle and von Vargha, *loc. cit.*) on further hydrolysis and osazone formation, but no sorbosazone was detected.

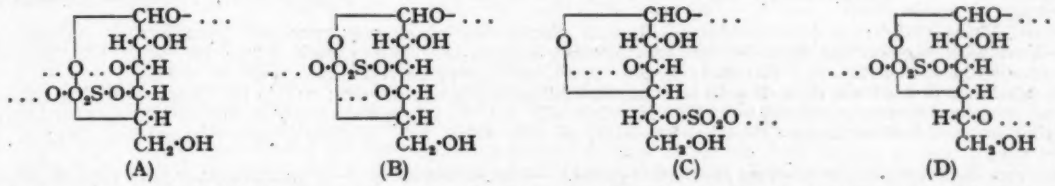


The corresponding 3-sulphate (V) would have given 2 : 3-anhydromethylallofuranosides (Peat and Wiggins, J., 1938, 1088), which should have yielded methylaltro- and methylgluco-furanosides. It is important to note the conclusion of Peat and Wiggins (J., 1938, 1810) that the proportion of methylaltrosides in the products of the alkaline hydrolysis of 2 : 3-anhydromethylallopyranosides is always far higher than that of the accompanying methylglucosides, in fact Robertson and Griffith (J., 1935, 1196) and Robertson and Dunlop (J., 1938, 472) were unable to isolate glucose derivatives in experiments of a similar nature. If ethylene oxide ring formation had taken place to any extent, therefore, on hydrolysis of (V) and suitable treatment allosazone should have been produced in sufficient quantity for recognition, but none was found. There is thus no evidence for the intermediate formation of ethylene oxide rings in the alkaline hydrolysis of (IV) and (V) and it is therefore held that the methylglucofuranosides (IX) are formed by the direct fission of the sulphate residues.

Part of the difficulty in obtaining a high yield of 3 : 6-anhydroglucosazone was found to be due to a *product*, m. p. 108—110°, which was isolated from the hydrolysis products of both the barium methylglucofuranoside-6-sulphate and the corresponding 3-sulphate after removal of the 3 : 6-anhydroglucosazone. This material appeared to be a hexosazone ($C_{18}H_{22}O_4N_4$). When carefully purified 3 : 6-anhydroglucose was subjected to osazone formation, however, of the total crude osazone obtained, *ca.* 20% was found to consist of the osazone usually designated 3 : 6-anhydroglucosazone, m. p. 187—189°, $[\alpha]_D^{17°}$ −151° in methanol, and about the same quantity of the osazone, m. p. 108—110°, which was isolated from (IV) and (V) was isolated from the mother-liquors. This substance must have been produced from 3 : 6-anhydroglucose in the products of hydrolysis of of the methylglucofuranosidesulphates (IV) and (V). Further work is in progress to determine the structure of this substance, which is most probably a hydrate of an anhydroglucosazone, although it is not necessarily directly related to the osazone, m. p. 187—189°. In any case it should be remembered that the structure of " 3 : 6-anhydroglucosazone," which appears to be identical with the anhydroglucosazone of Diels and Meyer

(*Annalen*, 1935, **519**, 157), has not yet been settled (Diels, Meyer, and Onnen, *ibid.*, 1936, **525**, 94; Percival and Percival, J., 1937, 1320).

Returning to the carragheen polysaccharide, four possible formulæ for the repeating unit were postulated (Buchanan, Percival, and Percival, *loc. cit.*) on the evidence of the isolation of 2 : 6-dimethyl galactose from methylated fractions; it may now be added that this polysaccharide does not react with periodic acid, showing the absence of α-glycol groups, which is in agreement with these suggestions and also eliminates certain other theoretical possibilities.



Of these four, (A) was chosen on the ground of the stability to alkali of the sulphate residue, for it was then considered that (B) and (D) would give 3 : 6-anhydrides and (C) a 5 : 6-anhydride with rapid elimination of the sulphate group. The present results show, however, that this particular argument cannot be supported for structure (C). There is no reason, however, why such a structure should not give rise to a 2 : 5-anhydro-ring, and in any event it is unlikely that the carragheen polysaccharide contains galactofuranose units, if the comparison of the rate of hydrolysis with acid with the galactocarolose of Haworth, Raistrick, and Stacey (*Biochem. J.*, 1937, **31**, 640), a polysaccharide containing galactofuranose units, is valid.

Formulation (A) for the major portion of the building units of the carragheen polysaccharide rests therefore on a sounder basis than hitherto, since experimental evidence has now been provided that 3 : 6-anhydride formation can take place when the sulphate residue is located on C_3, at any rate in glucose derivatives.

Experimental.

Barium Diacetone Glucofuranose-3-sulphate.—Pure diacetone glucose (8 g.) in dry pyridine (80 c.c.) was cooled to −18° and a solution of chlorosulphonic acid (4 c.c.) in alcohol-free chloroform (25 c.c.) was added during 2 hours so that the temperature never exceeded −15°. After standing overnight at room temperature, the mixture was again cooled to −18°, and a mixture of water (5 c.c.) and pyridine (20 c.c.) added. Dilution with water followed, after which the mixture was made alkaline to phenolphthalein with saturated barium hydroxide solution, the excess of alkali then being removed by carbon dioxide. After evaporation to *ca.* 100 c.c. at 35°/15 mm. in the presence of barium carbonate a slight excess of saturated silver sulphate solution was added, the solution filtered, and silver removed by hydrogen sulphide in the presence of barium carbonate, and the hydrogen sulphide by aeration. After the solution had been made alkaline with barium hydroxide and carbon dioxide passed in, filtration and evaporation in the presence of barium carbonate at 35°/15 mm. was followed by repeated extraction with boiling light petroleum (b. p. 40—60°; 500 c.c.) to remove unchanged diacetone glucose (0·3 g.). The residue was extracted with boiling acetone, filtered, and concentrated to 20 c.c. The addition of ether (200 c.c.), followed by filtration and evaporation, yielded a glass which crystallised in needles on solution in water and evaporation at room temperature. After being washed with alcohol and dried in a vacuum over phosphoric oxide, the product (6·0 g.) had $[\alpha]_D^{16°}$ −10·5° (*c*, 2·4, in water) [Found: Ba, 16·5; S, 7·6; $(CH_3)_2CO$, 26·5. Calc. for $(C_{12}H_{19}O_9S)_2Ba,H_2O$: Ba, 16·5; S, 7·7; $(CH_3)_2CO$, 27·9%].

Barium 1 : 2-*Monoacetone Glucofuranose-3-sulphate.*—Barium diacetone glucose-3-sulphate (3 g.) was kept for 3 hours at 15° with sulphuric acid (60 c.c., 0·5N), made alkaline to thymolphthalein with barium hydroxide, treated with carbon dioxide, filtered, and evaporated at 35°/15 mm. The crystalline product was recrystallised by solution in water (2 c.c.) and alcohol (4 c.c.), followed by the gradual addition, with scratching, to the warm solution, of a mixture of ether and alcohol (2 : 1) until crystallisation commenced. On standing at 0°, filtration, washing with alcohol and drying in a vacuum over phosphoric oxide, the *anhydrous* form of the product previously described by Ohle (*Biochem. Z.*, 1923, **136**, 428) as crystallising with four molecules of alcohol was obtained (2 g.) and had $[\alpha]_D^{16°}$ −15° (*c*, 1·5, in water) [Found: Ba, 18·8; S, 8·8; $(CH_3)_2CO$, 15·7. Calc. for $(C_9H_{15}O_9S)_2Ba$: Ba, 18·6; S, 8·7; $(CH_3)_2CO$, 15·8%].

Barium 1 : 2-*Monoacetone Glucofuranose-6-sulphate.*—1 : 2-Monoacetone glucofuranose was prepared from diacetone glucose (20 g.) by keeping for 210 minutes in sulphuric acid (280 c.c., 0·5N), followed by the addition of barium hydroxide in excess and treatment as previously described. The dry residue was extracted several times with boiling neutral ethyl acetate, after a preliminary extraction with ether to remove any unchanged diacetone glucose. The ethyl acetate extracts on cooling gave pure 1 : 2-monoacetone glucofuranose, m. p. 162°, $[\alpha]_D^{16°}$ −12° (*c*, 2·8, in water).

This material (11 g.) in dry pyridine (60 c.c.) was treated with chlorosulphonic acid (3·7 c.c.) in dry chloroform (35 c.c.) as for the diacetone glucose-3-sulphate except that after removal of hydrogen sulphide the solution was evaporated to dryness in the presence of barium carbonate, and the residue repeatedly extracted with boiling acetone (500 c.c.). These extracts were concentrated to 50 c.c. and the addition of dry ether (100 c.c.) caused the precipitation of a barium salt fraction (I) (8 g.), which was dried over phosphoric oxide in a vacuum and had $[\alpha]_D^{18°}$ −3·8° (*c*, 2·7, in water) [Found: Ba, 18·6; S, 8·4; $(CH_3)_2CO$, 15·0%].

The residue from the acetone extraction was extracted with water, and evaporation of the aqueous solution after filtration gave a further quantity (5 g.) of material (II), which had $[\alpha]_D^{16°}$ −4·0° (*c*, 3·0, in water) [Found: Ba, 18·9; S, 8·6; $(CH_3)_2CO$, 15·2. Calc. for $(C_9H_{15}O_9S)_2Ba$: Ba, 18·6; S, 8·7; $(CH_3)_2CO$, 15·8%].

Fractions (I) and (II) appear from the analytical results to be the *anhydrous* form of barium 1 : 2-monoacetone glucofuranose-6-sulphate described by Ohle (*loc. cit.*) as containing 1 molecule of alcohol. The purpose of extracting with acetone was to remove any unchanged monoacetone glucose. That any such contaminant was present in (II) is highly unlikely and the similarity of (I) to (II) shows that no appreciable amount was contained in (I).

Barium Methylglucofuranoside-3-sulphates.—Barium monoacetone glucose-3-sulphate (7 g.) in sulphuric acid (200 c.c.; 0·2N) was kept at 38° for 48 hours. An excess of barium carbonate was then added, and the neutral solution filtered and concentrated at 35°/15 mm., to yield a reducing glass, which was extracted twice with boiling alcohol in the presence of barium carbonate. After dissolution in water and precipitation in alcohol, a white powder (5·8 g.) was obtained having $[\alpha]_D^{20°}$ +29° (*c*, 2·2, in water) which was *barium glucose-3-sulphate* [Found: Ba, 20·3; S, 9·6. $(C_6H_{11}O_9S)_2Ba$

requires Ba, 20·95; S, 9·8%]. This substance (4·5 g.) was shaken with dry methanolic hydrogen chloride (80 c.c.; 1·2%) until dissolved, and the reaction stopped by the addition of barium carbonate after 22 hours; the specific rotation was then approximately zero, and the solution was almost non-reducing. After evaporation at 30°/15 mm., in the presence of barium carbonate in a large flask, the residue was extracted with water and treated with silver sulphate solution, followed by hydrogen sulphide and barium carbonate in the usual way. On evaporation a glass, $[\alpha]_D^{20°}$ −7° (*c*, 2·0, in water), was obtained, which was extracted repeatedly with cold ethyl acetate until no residue was obtained on evaporation of the extracts. The solid remaining was purified by dissolution in hot alcohol and precipitation in a large volume of anhydrous ether. The amorphous *product* (2·6 g.) had $[\alpha]_D^{20°}$ −4° (*c*, 2·4, in water) and was an αβ-mixture of barium methylglucofuranoside-3-sulphates [Found: Ba, 20·2; S, 9·2; OMe, 9·8. $(C_7H_{13}O_9S)_2Ba$ requires Ba, 20·1; S, 9·4; OMe, 9·1%].

Barium Methylglucofuranoside-6-sulphates.—Barium glucose-6-sulphate was prepared from barium monoacetone glucose-6-sulphate (6 g.) as described for the corresponding 3-sulphate. The product (4·6 g.) had $[\alpha]_D^{17°}$ +30° (*c*, 0·9, in water) (cf. Ohle, *loc. cit.*) [Found: Ba, 20·2; S, 9·5. Calc. for $(C_6H_{11}O_9S)_2Ba$: Ba, 20·95; S, 9·8%].

This substance (4·2 g.) was treated with methanolic hydrogen chloride (90 c.c.; 1·2%) for 26 hours to give, after the treatment described above, an amorphous *product* having $[\alpha]_D^{20°}$ +4° (*c*, 1·5, in water), which was an αβ-mixture of barium methylglucofuranoside-6-sulphates [Found: Ba, 19·6; S, 9·3; OMe, 9·6. $(C_7H_{13}O_9S)_2Ba$ requires Ba, 20·1; S, 9·4; OMe, 9·1%].

Hydrolysis Experiments with Sodium Hydroxide (2·83N).—The substance (0·2—0·3 g.) together with barium chloride (0·2 g.) was dissolved in sodium hydroxide solution (5 c.c.: 2·83N) in a tube of Jena glass. The mixture, protected by a condenser and a soda-lime tube, was heated in a boiling water-bath for the time stated; it was then cooled, cautiously acidified with acetic acid, and filtered through a weighed sintered Gooch crucible, to give a direct estimate of the barium sulphate formed (*a*). The filtrate was acidified with concentrated hydrochloric acid and boiled for 4 hours to complete the hydrolysis of the sulphate residues not removed by the alkali, and the barium sulphate (*b*) weighed in the usual way after the addition of barium chloride solution. A parallel experiment (*c*) was carried out on a weighed portion of the material under test, the alkaline hydrolysis being omitted. The results are expressed as the ratio of the weight of barium sulphate to the weight of starting material.

TABLE II.

	Time (hrs.).	*a*.	*b*.	*c*.	% Hydrolysis, 100*a*/*c*.	% Hydrolysis, 100 (1 − *b*/*c*).
Barium monoacetone glucose-6-sulphate	0·75	0·51	0·095	0·63	81	85
	1·5	0·53	0·085	,,	84	86·5
	3·5	0·57	0·04	,,	90·5	93·5
Barium monoacetone glucose-3-sulphate	16	0·02	0·62	0·64	3	3
	47	0·07	0·56	,,	11	12·5
Barium diacetone glucose-3-sulphate	15	0·01	0·545	0·56	2	3
	47	0·07	0·49	,,	12·5	12·5
Barium methylglucofuranoside-3-sulphates	0·82	0·40	0·28	0·67	60	58
	1·5	0·47	0·185	,,	70	73
	3·75	0·575	0·08	,,	86	88
Barium methylglucofuranoside-6-sulphates	0·5	0·375	0·31	0·68	55	54
	1·5	0·51	0·155	,,	75	77
	2·5	0·58	0·09	,,	85	87

Hydrolysis Experiments with Barium Hydroxide. Barium 1 : 2-*Monoacetone Glucofuranose-6-sulphate.*—Fraction II (4·0 g.) in water (150 c.c.) was heated for 15 hours at 100° with crystalline barium hydroxide (32 g.). Alcohol (150 c.c.) was then added, and the mixture cooled and filtered, the precipitate being washed several times with hot alcohol. Carbon dioxide was passed through the filtrate, which was then evaporated to dryness at 35°/15 mm. The residue was extracted with acetone, and removal of solvent gave a syrup (1·94 g.) which crystallised rapidly. After standing for some days and extraction with ether the crystalline material remaining (0·95 g.) consisted of 1 : 2-monoacetone glucofuranose, m. p. 158°, raised to 162° on recrystallisation from acetone–ether, not depressed by an authentic specimen, $[\alpha]_D^{17°}$ −11·8° (*c*, 3·0, in water). The ethereal extracts on evaporation gave a syrup (0·91 g.). A portion of the syrup (0·1 g.) was hydrolysed at 90° with 0·1N-sulphuric acid and treated with phenylhydrazine hydrochloride and sodium acetate. Needles of an osazone, m. p. 186°, were obtained, not depressed by 3 : 6-anhydroglucosazone.

The syrup crystallised completely after 2 weeks and was proved to be 1 : 2-monacetone 3 : 6-anhydroglucofuranose. Recrystallisation from ether–light petroleum gave needles, $[\alpha]_D^{16°}$ +29° (*c*, 1·3, in water), m. p. 55°, not depressed by an authentic specimen prepared from 1 : 2-monoacetone 5 : 6-ditosyl glucose (Ohle, v. Vargha, and Erlbach, *loc. cit.*).

The substance (0·7 g.) on hydrolysis with sulphuric acid (10 c.c., 0·1N) for 47 hours at 37° gave a crystalline product (0·45 g.), m. p. 121—122°, not depressed by an authentic specimen of 3 : 6-anhydroglucose, $[\alpha]_D^{17°}$ +53° (*c*, 1·5, in water).

In another experiment fraction (I) (4·5 g.) was hydrolysed for 19 hours as above to give after recrystallisation 1 : 2-monoacetone glucofuranose (0·88 g.) and 1 : 2-monoacetone 3 : 6-anhydroglucofuranose (0·82 g.).

Search for Idose Derivatives.—The mother-liquors from all the recrystallisations of the monoacetone glucofuranose (A) and the anhydro-compound (B) were hydrolysed separately and treated with phenylhydrazine acetate. Several crops of osazones were obtained from each and these were examined to see if *l*-sorbosazone was present.

Three crops of osazone (0·3 g.) from (A) had m. p. 192—195°, rising to 204° on recrystallisation, not depressed on admixture with glucosazone. An impure product, m. p. 175—180°, raised to 192° on recrystallisation, was obtained from the mother-liquor, but this was clearly not *l*-sorbosazone, m. p. 164°.

Two crops of osazone (0·2 g.) were obtained from (B), m. p. 160—178°, depressed to 140° on admixture with *l*-sorbosazone. Recrystallisation gave slightly impure 3 : 6-anhydroglucosazone, m. p. 182°, as the only identifiable product.

Barium 1 : 2-*Monoacetone Glucofuranose-3-sulphate.*—This substance (1·5 g.) in water (60 c.c.) was heated at 100° for 19 hours with barium hydroxide (10 g.). After removal of the excess of barium hydroxide, which partly crystallised on cooling, from solution by carbon dioxide, filtration and evaporation at 40°/15 mm. gave a product which contained no material extractable with boiling ether. The residue crystallised on treatment with water and on recrystallisation the starting material (1·0 g.), $[\alpha]_D^{18°}$ −14° (*c*, 2·0, in water), was obtained.

In a second experiment the crystalline barium salt (3 g.) in water (180 c.c.) was heated for 72 hours with barium hydroxide (33 g.) and treated as before. No ether-soluble products were obtained and recrystallisation of the residue from alcohol–water–ether gave the starting material (2·1 g.), $[\alpha]_D^{15°}$ −15° (*c*, 2·5, in water) (Found: Ba, 18·4%).

The mother-liquors were evaporated to give a solid which, when extracted with chloroform, gave a syrup (0·1 g.); this crystallised overnight and had m. p. 152°, raised to 162° on one recrystallisation, not depressed by monoacetone glucose.

Barium Diacetone Glucofuranose-3-sulphate.—Hydrolysis of this material (2·5 g.) as described above for 72 hours was followed by removal of barium hydroxide and evaporation at 40°/15 mm. The residue was extracted three times with boiling ether (200 c.c.); evaporation of the solution gave diacetone glucose (0·05 g.), m. p. 110°, $[\alpha]_D^{16°}$ −18·5° (*c*, 0·7, in water).

Barium Methylglucofuranoside-3-sulphates.—The substance (2·25 g.) in water (70 c.c.) was heated for 6 hours at 100° with crystalline barium hydroxide (20 g.) in an atmosphere of nitrogen, the subsequent working up being as described for the monoacetone-6-sulphate except that the residue, after the treatment with carbon dioxide, etc., was extracted with alcohol instead of acetone. By this means a syrup (0·81 g.; 67% of the theo.) was obtained (Found: OMe, 16·5%), $[\alpha]_D^{16°}$ +1° (*c*, 1·9, in 0·2N-sulphuric acid), rising to +45° after 7 hours at 100°. Neutralisation with barium carbonate, followed by evaporation and extraction with alcohol, etc., gave a reducing syrup (0·65 g.) which restored the colour to Schiff's reagent after 10 minutes.

Oxidation and Isolation of 3 : 6-*Anhydrogluconamide.*—The sugars (0·3 g.) in water (10 c.c.) were kept for 6 days with bromine (0·5 c.c.), which was then removed by aeration and the organic acids isolated in the usual way by neutralisation with silver carbonate, followed by treatment with hydrogen sulphide. The mixed acids in methanol were then esterified by excess of diazomethane dissolved in ether, and after removal of solvents the mixed esters were dissolved in saturated methanolic ammonia. After 2 days gluconamide (0·1 g.), m. p. 135°, raised to 144° on recrystallisation, was obtained. The mother-liquors after the removal of this amide crystallised to give an amide (0·05 g.), m. p. 148°, raised to 160° on recrystallisation, not depressed by 3 : 6-anhydrogluconamide. It showed $[\alpha]_D^{17°}$ +106° (*c*, 2·0, in water) (Found: N, 7·9. Calc. for $C_6H_{11}O_5N$: N, 7·9%).

Osazone Formation.—Another portion of the reducing sugars (0·3 g.) was treated with phenylhydrazine hydrochloride (0·6 g.), sodium acetate (1·0 g.), and sodium bisulphite (0·1 g.) in the usual way to give 3 crops of a crude osazone (0·25 g.), m. p. 130—195°. Glucosazone (0·12 g.), m. p. 209°, not depressed by an authentic specimen, separated on treatment with cold alcohol. The solution was allowed to evaporate, and the residue treated with warm acetonitrile. Crystals (0·02 g.), m. p. 185°, not depressed by 3 : 6-anhydroglucosazone, separated overnight (Found: N, 16·3. Calc. for $C_{18}H_{20}O_3N_4$: N, 16·5%).

The residue was recrystallised from aqueous alcohol several times to give an osazone (0·05 g.), m. p. 180—182°, m. p. 179° on admixture with 3 : 6-anhydroglucosazone (m. p. 187°), $[\alpha]_D^{18°}$ +140° (*c*, 0·3, in methanol), and was evidently mainly 3 : 6-anhydroglucosazone. The mother-liquors from which this material had been deposited, on warming and dilution with water deposited an *osazone* (0·01 g.), m. p. 107—109° (Found: N, 15·6. $C_{18}H_{22}O_4N_4$ requires N, 15·6%).

A second experiment on another portion (0·52 g.) of the reducing sugars obtained from barium methylglucofuranoside-3-sulphate gave a crude osazone (0·4 g.), from which glucosazone (0·20 g.), 3 : 6-anhydroglucosazone (0·07 g.), m. p. 186—187°, and the hexosazone (0·04 g.), m. p. 109°, but no other identifiable products were isolated. Special attention was paid to the fraction insoluble in cold alcohol, but this proved to be entirely glucosazone and no product obtained on fractional crystallisation resembling allosazone (m. p. 178°) could be detected, since no fraction had a m. p. lower than 205°.

Barium Methylglucofuranoside-6-sulphates.—The substance (3·5 g.) was hydrolysed with barium hydroxide as described above to give a syrupy mixture of methylglycosides (1·3 g.; OMe, 16·3%), $[\alpha]_D^{18°}$ +10° (*c*, 2·0, in 0·2N-sulphuric acid), raised to +50° on heating for 8 hours at 100°. The free sugars (1·0 g.) so obtained rapidly restored the colour to Schiff's reagent.

Isolation of 3 : 6-*Anhydrogluconamide.*—The bromine oxidation of 0·3 g. gave, on the treatment previously described, gluconamide (0·1 g.) and 3 : 6-anhydrogluconamide (0·06 g.), m. p. 159°, not depressed by an authentic specimen, $[\alpha]_D^{17°}$ +108° (*c*, 1·0, in water).

Osazone Formation.—The reducing sugars (0·6 g.) gave a crude osazone (0·47 g.), m. p. 160—200°, from which pure glucosazone (0·24 g.) was isolated on treatment with cold alcohol, 3 : 6-anhydroglucosazone (on treatment with acetonitrile as before), (0·03 g.), m. p. 187°, not depressed by an authentic specimen, and the hexosazone (0·05 g.), m. p. 108—110°, not depressed by the specimen prepared from the 3-sulphate.

The remaining osazone (0·1 g.) at one stage of its purification had m. p. 162—165°, but that it was not *l*-sorbosazone was shown by the fact that the m. p. fell to 135° on admixture with a specimen of that substance. On further recrystallisation (0·06 g.) the m. p. was raised to 176°, m. p. 174° on admixture with 3 : 6-anhydroglucosazone, $[\alpha]_D^{17°}$ −140° (*c*, 0·25, in methanol) (Found: N, 16·4%). This fraction was therefore mainly 3 : 6-anhydroglucosazone. From the mother-liquors the osazone (0·01 g.), m. p. 110°, was isolated.

Osazone Formation with Pure 3 : 6-*Anhydroglucose.*—3 : 6-Anhydroglucose (0·5 g.), m. p. 120—121°, thrice recrystallised in water (20 c.c.) was heated for 4 hours with phenylhydrazine hydrochloride, sodium acetate and sodium bisulphite in the usual way. The crude osazone (0·56 g.) had m. p. 140—180°. Treatment with cold alcohol gave prisms (0·11 g.), m. p. 185—186°, raised to 187—188° on recrystallisation, $[\alpha]_D^{17°}$ −134° (*c*, 0·4, in ethanol), −150° (*c*, 0·4 in methanol) (Found: C, 63·2; H, 6·0; N, 16·4. Calc. for $C_{18}H_{20}O_3N_4$: C, 63·5; H, 5·9; N, 16·5%).

The alcoholic solution from which these crystals separated was warmed to 70° and diluted with water to turbidity; cooling gave an osazone, m. p. 177°, raised to 180—182° on recrystallisation. This product (0·2 g.) had not the crystalline form of the first product but appeared to consist of aggregates. Nevertheless the specific rotation was $[\alpha]_D^{18°}$ −147° (*c*, 0·4, in methanol) and the m. p. was not depressed on admixture with the first specimen. The filtrates from the recrystallisations, on warming and dilution with water, gave a pale yellow osazone (0·11 g.), flaky when dry, m. p. 106°, raised to 108—110° on recrystallisation, not depressed by the specimens prepared above from the methylglucofuranoside-3- and -6-sulphates (Found: C, 60·2; H. 5·9; N, 15·5. $C_{18}H_{22}O_4N_4$ requires C, 60·2; H, 6·2; N, 15·6%).

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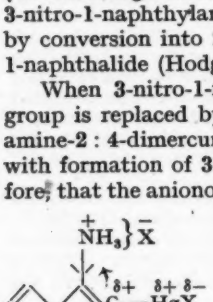
32. *Reactions of 3-Nitro-1-naphthylamine. Part II. Chlorination, Mercuration, Coupling with Diazo-compounds, and the Preparation of some Arsenicals.*

By HERBERT H. HODGSON and DAVID E. HATHWAY.

3-Nitroaceto-1-naphthalide is monochlorinated in position 4, whereas 3-nitro-1-naphthylamine is mercurated initially in position 2 and subsequently in position 4; it couples with certain diazo-compounds also in position 2. The influence of the 3-nitro-group on the deactivation of the 4-position is briefly discussed. The preparation of some arsenicals is described.

THE reaction of chlorine with 3-nitro-1-naphthylamine is very complex, but 3-nitroaceto-1-naphthalide, like 3-nitroacetanilide, is monochlorinated by elementary chlorine in position 4, the constitution of the resulting *4-chloro-3-nitroaceto-1-naphthalide* being established by its conversion into 1 : 4-dichloro-2-nitronaphthalene (Hodgson and Crook, J., 1936, 1502). On the other hand, 3-nitro-1-naphthylamine is readily mercurated in position 2 when stoicheiometric quantities of the amine and mercuric acetate are boiled together in aqueous alcohol, the resulting *3-nitro-1-naphthylamine-2-mercuriacetate* being converted by a solution of iodine in aqueous potassium iodide into *2-iodo-3-nitro-1-naphthylamine*, which on deamination gives 3-iodo-2-nitronaphthalene (cf. Cumming and Howie, J., 1931, 3178). By the same procedure with double the amount of mercuric acetate, 3-nitro-1-naphthylamine gives *3-nitro-1-naphthylamine-2 : 4-dimercuriacetate*, whose constitution is established by conversion into 2 : 4-diacetoxymercuri-3-nitroaceto-1-naphthalide, from which 2 : 4-dibromo-3-nitroaceto-1-naphthalide (Hodgson and Hathway, J., 1944, 21) is obtained by treatment with bromine.

When 3-nitro-1-naphthylamine-2-mercuriacetate is ground with hydrobromic acid (*d* 1·6), the mercuri-group is replaced by hydrogen with regeneration of 3-nitro-1-naphthylamine, and when 3-nitro-1-naphthylamine-2 : 4-dimercuriacetate is refluxed with 90% formic acid, both mercuri-groups are replaced by hydrogen with formation of 3-nitroformo-1-naphthalide (Hodgson and Birtwell, J., 1944, 75). It would appear, therefore, that the anionoid character of both the 2- and the 4-carbon atom is so enfeebled by the combined kationoid effects of the 3-nitro-group and salt formation at the amino-group that the kationoid mercury is unable to resist anionoid attack by either the hydrobromic or formic acid with consequent replacement of the mercuri-group by hydrogen (cf. also Pauling, "Nature of the Chemical Bond," 1941, 199, on the adjacent charge rule).



X = Br, H·CO·O

Diazotised *p*-nitroaniline, *p*-chloroaniline, and aniline couple in acetic acid–ethyl alcohol solution with 3-nitro-1-naphthylamine to give monoazo-compounds in yields of 97%, 50%, and 7% respectively. The fact that in each case the aminoazo-compound can be neither acetylated nor diazotised constitutes evidence in favour of coupling in position 2, since 4-azo-1-naphthylamines are all readily acetylated and diazotised (cf. Morgan and Jones, *J. Soc. Chem. Ind.*, 1923, **42**, 341 T; Hodgson and Turner, J., 1943, 393). The colours of *3-nitro-2-p-chlorobenzeneazo-1-naphthylamine* with sulphuric acid of different strengths suggest varying salt formation. Also when sodium hydroxide is added to the scarlet solutions of all the dyes in acetone, the colour change to pronounced purple indicates salt formation by the alkali (cf. Chattaway and Clemo, J., 1923, **123**, 3041).

Diazo-coupling in position 2 and yield variation of the monoazo-compounds formed in order of the decreasing positivity of the diazo-reagent (cf. Robinson, "Outline of an Electrochemical Theory of the Course of Organic Reactions," Institute of Chemistry, 1932, p. 42) emphasise the enfeebling effect of the 3-nitro-group on the anionoid character of the 4-position, a result supported by monomercuration in position 2. The coupling of 3-nitro-1-naphthylamine in position 2 falls into line with the coupling of 1-naphthylamine-3-sulphonic acid in position 2 (Gattermann and Schulze, *Ber.*, 1897, **30**, 50; Gattermann and Liebermann, *Annalen*, 1912, **393**, 198), and though in some cases mixtures of 2- and 4-coupled compounds are formed, the former preponderate.

3-Nitro-1-naphthylamine is converted by the Bart reaction (*Annalen*, 1922, **429**, 95) into *3-nitro-1-naphthylarsonic acid*, which is reduced by ferrous hydroxide (Benda, *Ber.*, 1911, **44**, 3302) to *3-amino-1-naphthylarsonic acid* as shown by diazotisation and subsequent coupling with β-naphthol to give a crimson dye.

The fact that an aqueous solution of sodium bicarbonate decomposes on warming would appear to suggest that sodium carbonate could be used in the sodium sulphide mixture for the mono-reduction of 1 : 3-dinitronaphthalene (Hodgson and Birtwell, J., 1944, 75). When this was done, however, the yield of mixed nitronaphthylamines fell from 85% to 40%, and 95% of it was 3-nitro-1-naphthylamine, whereas when sodium bicarbonate was used the composition was 84% of 3-nitro-1- and 16% of 4-nitro-2-naphthylamine. The rôle of the bicarbonate as suggested by Hodgson and Birtwell (*loc. cit.*) is thus not only to buffer the reduction mixture throughout the reaction but also to liberate the active reducing agent NaSH according to the equation $NaHCO_3 + Na_2S = NaSH + Na_2CO_3$. Incidentally, carbon dioxide is not evolved when an aqueous solution of sodium bicarbonate and sodium sulphide is heated.

EXPERIMENTAL.

Chlorination of 3-Nitroaceto-1-naphthalide.—A finely divided suspension of 3-nitroaceto-1-naphthalide, formed by refluxing 3-nitro-1-naphthylamine (10 g.) with acetic anhydride (7 c.c.) and glacial acetic acid (120 c.c.) for 15 minutes, was treated with a brisk current of dry chlorine on the boiling water-bath for 90 minutes. *4-Chloro-3-nitroaceto-1-naphthalide* (6 g.), which separated on cooling (scratching), crystallised from glacial acetic acid in colourless needles, m. p. 235° (Found : Cl, 13·7. $C_{12}H_9O_3N_2Cl$ requires Cl, 13·4%). It was (4·2 g.) refluxed for 3 hours with 50% sulphuric acid (60 c.c.) and ethyl alcohol (75 c.c., charcoal), and the mixture poured into ice-water : *4-chloro-3-nitro-1-naphthylamine* (4·2 g.), precipitated by ammonia, crystallised from aqueous ethyl alcohol in yellow needles, m. p. 128° (Found : Cl, 15·7. $C_{10}H_7O_2N_2Cl$ requires Cl, 16·0%).

4-Chloro-3-nitroformo-1-naphthalide, prepared by refluxing the above amine with 90% formic acid, crystallised from alcohol in colourless felted needles, m. p. 230° (Found : N, 11·3. $C_{11}H_7O_3N_2Cl$ requires N, 11·2%).

Proof of Chlorination in Position 4.—The 4-chloro-3-nitro-1-naphthylamine (1·8 g.), dissolved in glacial acetic acid (15 c.c.), was stirred below 20° into a solution of sodium nitrite (0·8 g.) in sulphuric acid (10 c.c., *d* 1·84), and the mixture stirred after 15 minutes with a suspension of red cuprous oxide (1 g.) in methyl alcohol (50 c.c.); the temperature then rose to 70°. The mixture was poured into ice-water (500 c.c.), and the solid removed, washed free from copper salts, and dried (pump). 1-Chloro-2-nitronaphthalene, extracted from it with boiling alcohol and recovered from the extract by steam-distillation, crystallised from methyl alcohol (charcoal) in pale yellow needles (1 g.), m. p. 76° (Hodgson and

Kilner, J., 1926, 8, give m. p. 76°). Another solution of the diazonium sulphate, prepared as above from the amine (1·8 g.), was stirred into a solution of cuprous chloride (2·5 g.) in hydrochloric acid (10 c.c., *d* 1·18); the precipitated 1 : 4-dichloro-2-nitronaphthalene (2 g.) was removed, extracted, and crystallised from glacial acetic acid, forming yellow needles, m. p. 117° (Hodgson and Crook, J., 1936, 1502, give m. p. 116·5°).

Monomercuration of 3-Nitro-1-naphthylamine.—No mercuriacetate could be isolated when a glacial acetic acid solution of 3-nitro-1-naphthylamine and mercuric acetate in stoicheiometric proportion was refluxed. Monomercuration was effected when a solution of mercuric acetate (12·8 g.) in water (50 c.c.) to which glacial acetic acid (2 c.c.) had been added was mixed with a solution of 3-nitro-1-naphthylamine (7·6 g.) in alcohol (100 c.c.), and the mixture boiled until the supernatant liquor gave no reaction with ammonium sulphide for inorganic mercury (*ca.* 1 hour). The liquid was then filtered hot, and the precipitate of *3-nitro-1-naphthylamine-2-mercuriacetate* (14 g.) washed with boiling aqueous alcohol; it crystallised from 25% acetic acid in brown micro-needles, which began to decompose at *ca.* 200° (Found : Hg, 45·3. $C_{12}H_{10}O_4N_2Hg$ requires Hg, 45·0%). A finely divided suspension of the monomercuriacetate (4·5 g.) in 20% potassium iodide solution (40 c.c.), to which a little alcohol had been added, was refluxed with 20% potassium iodide solution (40 c.c.) containing iodine (2·7 g.) for 45 minutes. On cooling, the *2-iodo-3-nitro-1-naphthylamine* (1 g.) was removed, washed with water and aqueous sodium thiosulphate, and extracted with ethyl alcohol containing charcoal and sodium thiosulphate; it crystallised from the filtered extract in micro-plates, m. p. 100° (Found : I, 40·0. $C_{10}H_7O_2N_2I$ requires I, 40·4%). A solution of 2-iodo-3-nitro-1-naphthylamine (1 g.) in glacial acetic acid (10 c.c.) was diazotised by addition below 20° to sulphuric acid (5 c.c., *d* 1·84), in which sodium nitrite (0·35 g.) had been dissolved. The cold solution of the diazonium sulphate was stirred into a suspension of red cuprous oxide (1 g.) in methyl alcohol (20 c.c.) and stirring was continued until the reaction had ceased. The mixture was poured into ice-water (200 g.), the methyl acetate layer removed by evaporation, and the precipitate collected and refluxed with ethyl alcohol containing charcoal and aqueous sodium thiosulphate; after filtration, the 3-iodo-2-nitronaphthalene (0·4 g.) in the filtrate was precipitated by the addition of ice-water, and crystallised from aqueous alcohol, forming rosettes of golden plates, m. p. 92° (Found : I, 42·2. Calc. : I, 42·5%) (Cumming and Howie, J., 1931, 3178, report yellow prisms from alcohol, m. p. 89·5°, after many recrystallisations).

2-Halogenomercuri-3-nitro-1-naphthylamines.—Hot 20% aqueous potassium chloride, bromide, and iodide reacted with the monomercuriacetate to give the following crystalline 2-halogenomercuri-3-nitro-1-naphthylamines :

Compound.	M. p. (decomp.).	Colour.	Crystal form.	% Hg. Found.	Calc.
Chloro-	190°	Rust	Rods	47·1	47·4
Bromo-	214	Tan	Needles	42·5	42·9
Iodo-	204	Red-brown	Squat rods	38·7	39·0

20% Aqueous potassium hydroxide gave *2-hydroxymercuri-3-nitro-1-naphthylamine*, which crystallised in long brown needles, m. p. 212° (decomp.) (Found : Hg, 50·0. $C_{10}H_8O_3N_2Hg$ requires Hg, 49·6%).

The action of hydrobromic acid (*d* 1·6) on 3-nitro-1-naphthylamine-2-mercuriacetate was to give 3-nitro-1-naphthylamine hydrobromide, which was basified to give 3-nitro-1-naphthylamine, m. p. and mixed m. p. 136°.

Dimercuration of 3-Nitro-1-naphthylamine.—A solution of mercuric acetate (13·2 g.) in water (50 c.c.) to which glacial acetic acid (2 c.c.) had been added was added to a solution of 3-nitro-1-naphthylamine (3·8 g.) in alcohol (60 c.c.), and the mixture boiled (*ca.* 3 hours) until the supernatant liquor gave no reaction for inorganic mercury when tested with ammonium sulphide; it was filtered hot, and the precipitate washed with boiling alcohol and extracted with boiling glacial acetic acid. The residue (insoluble in organic solvents) consisted of chestnut felted needles of *3-nitro-1-naphthylamine-2 : 4-dimercuriacetate* (12·5 g.), m. p. 210° (decomp.) (Found : Hg, 56·4. $C_{14}H_{13}O_8N_2Hg_2$ requires Hg, 56·8%). When refluxed with 90% formic acid and filtered, the dimercuriacetate gave 3-nitroformo-1-naphthalide, which separated from the filtrate and recrystallised from ethyl alcohol in fine yellow crystals, m. p. and mixed m. p. with an authentic specimen, 216°. When the dimercuriacetate (4 g.) was refluxed with a mixture of ethyl acetate (60 c.c.) and acetic anhydride (15 c.c.) for 10 hours (the reaction was considered complete when the brown solid had completely dissolved), 2 : 4-diacetoxymercuri-3-nitroaceto-1-naphthalide (2·5 g.) separated from the liquor in greenish-yellow needles, which had no definite m. p., but decomposed on heating (since mercury was formed in the reaction, the substance was not analysed). This compound (1·9 g.) was converted, when shaken with a solution of bromine (0·85 g.) in aqueous 20% potassium bromide (80 c.c.) and a little alcohol, at 40°, into 2 : 4-dibromo-3-nitroaceto-1-naphthalide (0·8 g.), which crystallised from glacial acetic acid in colourless needles, m. p. and mixed m. p. 202° (Hodgson and Hathway, *loc. cit.*), and was hydrolysed by refluxing for 3 hours with a mixture of 50% sulphuric acid (10 c.c.) and ethyl alcohol (12 c.c.) to give, on pouring into ice-water, 2 : 4-dibromo-3-nitro-1-naphthylamine sulphate, which, on basification and crystallisation from ethyl alcohol, gave small bright yellow plates of 2 : 4-dibromo-3-nitro-1-naphthylamine, m. p. and mixed m. p. 182° (Hodgson and Hathway, *loc. cit.*).

Coupling of 3-Nitro-1-naphthylamine with Diazotised Amines in Acetic Acid.—A chilled solution of *p*-nitroaniline (2·76 g.) in hydrochloric acid (9 g., *d* 1·18) and water (14 c.c.) was diazotised below 5° by aqueous sodium nitrite (1·4 g.), and the filtered solution neutralised with sodium acetate (7 g. in a little water) and stirred dropwise into a solution of 3-nitro-1-naphthylamine (3·76 g.) in ethyl alcohol (200 c.c.) below −5°. As coupling proceeded, aqueous sodium acetate was added so that the medium was never acid to Congo-red paper. The mixture was stirred until coupling was complete. The *3-nitro-2-p-nitrobenzeneazo-1-naphthylamine* (6·8 g., 97% yield) was removed, washed with water, and dried at 50°; it crystallised from toluene in brick-red micro-needles and from glacial acetic acid in large crimson needles, m. p. 250° (Found : N, 20·7. $C_{16}H_{11}O_4N_5$ requires N, 20·8%), which gave a purple colour with concentrated sulphuric acid, changing to scarlet on dilution. The scarlet solution in acetone changed to indigo-violet on addition of aqueous sodium hydroxide, and warm ethyl-alcoholic potassium hydroxide produced a deep purple solution.

3-Nitro-2-p-chlorobenzeneazo-1-naphthylamine, prepared in 50% yield with diazotised *p*-chloroaniline (0·01 g.-mol.) as above and crystallised successively from toluene and glacial acetic acid, formed four-sided orange plates having a steel-blue lustre, m. p. 188° (Found : Cl, 10·8. $C_{16}H_{11}O_2N_4Cl$ requires Cl, 10·9%), which gave a deep scarlet colour with sulphuric acid, changing on dilution with water to purple, thence to scarlet, and finally to bright yellow; the orange solution in acetone became wine-red on addition of aqueous sodium hydroxide, and alcoholic potash afforded a wine-red solution.

3-Nitro-2-benzeneazo-1-naphthylamine was obtained in only 7% yield by coupling diazotised aniline (0·01 g.-mol.) with 3-nitro-1-naphthylamine, as above; crystallised successively from toluene and acetic acid, it formed scarlet micro-needles, m. p. 275° (Found : N, 19·2. $C_{16}H_{12}O_2N_4$ requires N, 19·2%), which gave a purple colour with concentrated sulphuric acid, changing to scarlet on dilution.

Monoreduction of 1 : 3-Dinitronaphthalene by Sodium Sulphide and Sodium Carbonate.—The amine (13·5 g.), dissolved in boiling methyl alcohol (240 c.c.), was agitated while sodium sulphide (26 g.) and sodium carbonate (4·5 g.) in water (6·3 c.c.) were added during 30 minutes. The mixture was then poured into ice-water (2000 g.), and the precipitate

collected and extracted with 6% hydrochloric acid (600 c.c.) to remove 3-nitro-1- and 4-nitro-2-naphthylamine, which were precipitated from the extract by ammonia. Yield 5·5 g., m. p. 126°, indicating 95% of 3-nitro-1-naphthylamine according to the thermal diagram of Hodgson and Hathway (J., 1944, 386).

Preparation of Arsenicals from 3-Nitro-1-naphthylamine.—*3-Nitro-1-naphthylarsonic acid.* A finely divided suspension of 3-nitro-1-naphthylamine hydrochloride, prepared by rapid cooling of a solution of the base (9·4 g.) in 6% hydrochloric acid (350 c.c.) with vigorous agitation, was treated at 15—20° with an aqueous solution of sodium nitrite (5 g.), and to the clear solution of the diazonium chloride at 0° were added simultaneously (*a*) a solution of sodium meta-arsenite (20 g.) and a few crystals of copper sulphate in ice-water (1 l.) and (*b*) 20% aqueous sodium hydroxide (100 c.c.) at such a rate that the resulting solution remained slightly alkaline throughout. The mixture was stirred for several hours, concentrated, and filtered, the filtrate acidified to Congo-red paper, and the precipitate of *3-nitro-1-naphthylarsonic acid* (6 g., 42%) removed, washed, and purified by precipitation with acid from aqueous sodium carbonate solution. It crystallised from water containing a little alcohol in pale orange rods which decomposed on heating (Found: N, 4·7; As, 25·0. $C_{10}H_8O_5NAs$ requires N, 4·7; As, 25·3%).

3-Amino-1-naphthylarsonic acid. 25% Aqueous sodium hydroxide was added to a solution of crystalline ferrous sulphate (27 g.) in water (80 c.c.) until the precipitate after shaking reacted strongly alkaline to litmus; a solution of 3-nitro-1-naphthylarsonic acid (4 g.) in 5% aqueous sodium hydroxide was then added, and the mixture shaken for 10 minutes. The precipitate was removed and washed, the bulked filtrates just acidified with mineral acid to Congo-red paper, and the excess of mineral acid removed by aqueous sodium acetate. *3-Amino-1-naphthylarsonic acid*, extracted from the precipitate with boiling alcohol, crystallised from aqueous alcohol in colourless felted needles, m. p. 252° (decomp.) (Found: As, 27·8. $C_{10}H_{10}O_3NAs$ requires As, 28·1%).

3-Acetamido-1-naphthylarsonic acid crystallised from glacial acetic acid in colourless needles, which decomposed on heating (Found: N, 4·5. $C_{12}H_{12}O_4NAs$ requires N, 4·5%).

1-Arsono-3-p-nitrobenzylidenenaphthylamine was obtained when stoicheiometric quantities of the above amino-arsonic acid and *p*-nitrobenzaldehyde were refluxed in acetic acid; it crystallised from glacial acetic acid in yellow needles, which decomposed on heating (Found: N, 7·2. $C_{17}H_{13}O_5N_2As$ requires N, 7·0%).

1-Arsononaphthalene-3-azo-β-naphthol was obtained when a finely divided paste of the above amine (0·35 g.) in glacial acetic acid (4 c.c.) was diazotised by addition below 20° to a solution of sodium nitrite (0·15 g.) in sulphuric acid (2·5 c.c., *d* 1·84), and the solution of the diazonium sulphate added to one of β-naphthol (0·2 g.) in 20% aqueous sodium hydroxide (35 c.c.) and water (17 c.c.) below 20°. After 2 hours' stirring, the dye was precipitated (0·5 g., 90% yield) with hydrochloric acid. It crystallised from acetone in crimson micro-needles which decomposed on heating (Found: N, 6·8. $C_{20}H_{15}O_4N_2As$ requires N, 6·6%), and gave a magenta colour with concentrated sulphuric acid which changed on dilution to scarlet.

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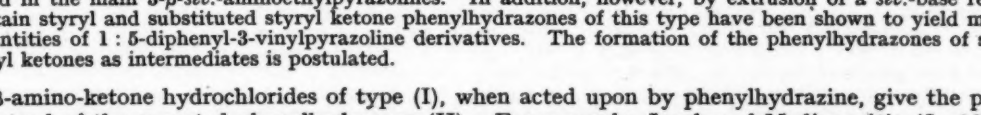
33. *Pyrazoline Ring Formation. Part I. The Action of Phenylhydrazine on Some Saturated and Unsaturated β-Amino-ketones.*

By HUGH B. NISBET.

Phenylhydrazine, acting on *β-sec.*-aminoethyl ketones in the form of their hydrochlorides, gives first the phenylhydrazone, which by extrusion of a *sec.*-base residue yields a pyrazoline derivative. Examination of the possible reaction mechanisms suggests the intermediate formation of a vinyl derivative which undergoes prototropic rearrangement to the pyrazoline.

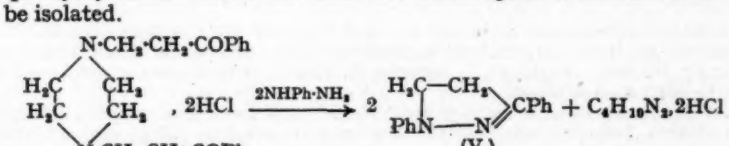
The phenylhydrazones of α-unsaturated *β-sec.*-aminoethyl ketone hydrochlorides on treatment with acid yield in the main 3-*β-sec.*-aminoethylpyrazolines. In addition, however, by extrusion of a *sec.*-base residue certain styryl and substituted styryl ketone phenylhydrazones of this type have been shown to yield minute quantities of 1 : 5-diphenyl-3-vinylpyrazoline derivatives. The formation of the phenylhydrazones of styryl vinyl ketones as intermediates is postulated.

MANY β-amino-ketone hydrochlorides of type (I), when acted upon by phenylhydrazine, give the pyrazoline (III) instead of the expected phenylhydrazone (II). For example, Jacob and Madinaveitia (J., 1937, 1929) showed that, warmed with phenylhydrazine in a solution of sodium acetate in 50% acetic acid, the hydrochlorides of β-dimethylaminopropiophenone (I; R = Ph, R′ = Me) and methyl β-dimethylaminoethyl ketone



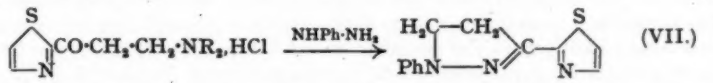
(I.) (II.) (III.)

(I; R and R′ = Me) gave 1 : 3-diphenyl- and 1-phenyl-3-methyl-pyrazoline respectively. Although the intermediate phenylhydrazones were not prepared by these workers, that such compounds are formed has now been proved by the isolation of the *phenylhydrazones* of β-dimethylaminopropiophenone hydrochloride and of β-piperidylpropiophenone hydrochloride (II; R = Ph, R′ = NC_5H_{10}) by the method of Auwers and Voss (*Ber.*, 1909, **42**, 4411) and it has been shown that both are converted into 1 : 3-diphenylpyrazoline by warming with a solution of sodium acetate in 50% acetic acid. Moreover, 1 : 4-bis-β-benzoylethylpiperazine dihydrochloride (IV) with phenylhydrazine under the same conditions gives a mixture from which 1 : 3-diphenylpyrazoline (V) can be isolated.



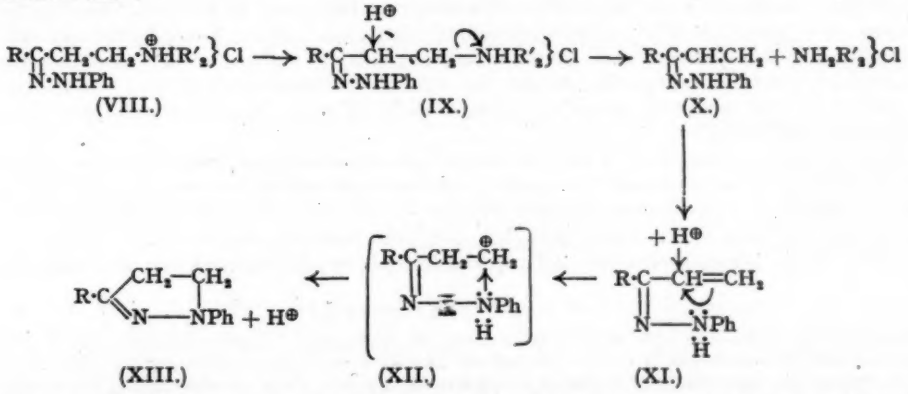
(IV.) (V.)

Levvy and Nisbet (J., 1938, 1053) record the formation of 1-phenyl-3-thiazylpyrazoline (VII) in attempts to prepare the phenylhydrazones of similar β-aminoketone hydrochlorides (VI) derived from 2-acetyl-4-phenylthiazole by the Mannich reaction :

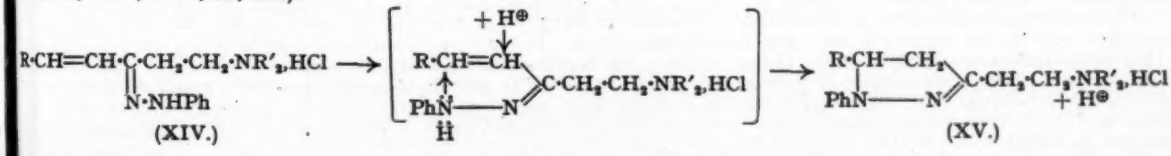


and Harradence and Lions (*J. Proc. Roy. Soc. N.S. Wales*, 1939, **72**, 233) observed the formation of pyrazolines from phenylhydrazine and several aryl β-morpholinoethyl ketones and β-morpholinoethyl 2-thienyl ketone.

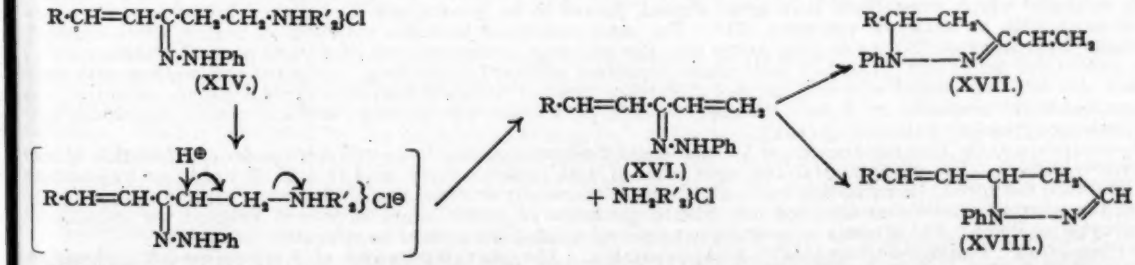
All the pyrazolines, so formed, are obtained by the extrusion of a secondary base residue, followed by ring closure. Among the mechanisms which can be suggested for this reaction the most probable is one which postulates initiation of the change by propagation of the instability originating in the ammonium group (VIII) to a hydrogen atom attached to the β-carbon atom (IX). This hydrogen extruded as a proton would initiate a series of changes which result in the production of an unsaturated linkage in the αβ-position (X). An intramolecular protropic change initiated by semi-polar activation of the double bond (XI) and completed by electron donation from the nitrogen atom and extrusion of a proton (XII and XIII) would bring about the pyrazoline ring formation thus :



The isomerisation in acid solution of the phenylhydrazones of αβ-unsaturated β'-dialkylaminoethyl ketone hydrochlorides of type (XIV) has been used extensively in the formation of 3-β-substituted aminoethylpyrazolines (XV) (Nisbet, J., 1938, 1237, 1568, 1572), the salts of which have been shown to have considerable efficacy as surface local anæsthetics (Sinha, *J. Pharm. Exp. Ther.*, 1936, **57**, 199; 1939, **66**, 54; Levvy and Nisbet, *ibid.*, 1939, **65**, 129).



Examination of the formula for these phenylhydrazones (XIV), however, indicates the possibility that pyrazoline formation may be achieved by another route, for if the styryl group is regarded as the group R in compounds of type (I), formation of the pyrazoline of type (III) by extrusion of the secondary base residue cannot be excluded. If the mechanism postulated for the extrusion of this residue be accepted, the intermediate (XVI), which is the phenylhydrazone of a styryl vinyl ketone, will be formed. This, by intramolecular prototropic change, would give rise to either or both the isomeric pyrazolines (XVII) and (XVIII).



Nothing appears to be known regarding the rearrangement of phenylhydrazones of styryl vinyl ketones, but Raiford and his collaborators (*J. Amer. Chem. Soc.*, 1933, **55**, 1125; 1934, **56**, 174) have shown that, in the phenylhydrazones of unsymmetrically substituted dibenzylideneacetones, where one of the benzene nuclei

carries an electron-attracting group, such as nitro, ring closure involves the unsaturation further away from that nucleus. Conversely, also, they show that where a nucleus carries an electron-donating group, such as *p*-methoxy, the unsaturation nearer this nucleus is involved in ring closure. If the same conditions apply to the rearrangement of the phenylhydrazones of styryl vinyl ketones, the resulting pyrazoline formed by the extrusion of the secondary base residue from compounds of type (XIV) in the cases studied is more likely to be the vinylpyrazoline (XVII) than the isomeric styryl compound (XVIII), for the presence of an electron-donating group such as phenyl, *p*-methoxyphenyl or methylenedioxyphenyl, as a constituent of the styryl radical is more likely to have the styryl unsaturation activated for intramolecular prototropic change than the vinyl group.

Although it has not been possible to investigate the whole range of reactions utilised in the earlier work on the formation of 3-β-dialkylaminoethylpyrazoline salts, certain selected cases have been examined and sufficient evidence accumulated to show that extrusion of a secondary base residue, followed by ring closure, does occur to a minute extent in many cases simultaneously with the normal isomerisation of phenylhydrazones of type (XIV).

For the reasons stated above, the new compounds are tentatively assigned the constitution of 3-vinylpyrazolines. Their exact constitution is amenable to determination by oxidation and reduction processes combined with alternative synthesis, and it is hoped to report on these at a later date when conditions are favourable for continuance of this work. Meantime, it has been found that isomerisation of the phenylhydrazones of 1-piperidino-5-(3′ : 4′-methylenedioxyphenyl)-Δ^4-penten-3-one hydrochloride and of the corresponding 5-*p*-anisyl derivative give predominating yields of 1-phenyl-5-(3′ : 4′-methylenedioxyphenyl)-3-β-piperidinoethylpyrazoline hydrochloride and the 5-*p*-anisyl derivative, but that minute traces are formed of compounds at present assigned the constitutions of 5-(3′ : 4′-*methylenedioxyphenyl*)- and 5-p-*anisyl*-1-*phenyl*-3-*vinylpyrazoline* respectively.

Phenylhydrazine, acting on 1-(*di*-β-*hydroxyethyl*)*amino*-5-*phenyl*-Δ^4-*penten*-3-*one hydrochloride* and on *dicinnamylethylpiperazine hydrochloride*, gives mixtures from which by isomerisation with dilute acetic acid the same compound 1 : 5-*diphenyl*-3-*vinylpyrazoline* is obtained in minute quantities by extrusion of the secondary base residues. This compound has not been isolated, as one might expect it should be, in the isomerisation of the phenylhydrazone of 1-piperidino-5-phenyl-Δ^4-penten-3-one hydrochloride.

Experimental.

1-*Di*-(β-*hydroxyethyl*)*amino*-5-*phenyl*-Δ^4-*penten*-3-*one Hydrochloride*.—Diethanolamine (10·5 g.) was dissolved in ethyl alcohol (20 ml.) and concentrated hydrochloric acid (8·9 ml.), benzylideneacetone (14·6 g.) added, the mixture heated to boiling, paraformaldehyde added in two portions (3 g. and 1·5 g.), and refluxing continued after each addition until the mixture was homogeneous. After about 10 mins., the reaction mixture was filtered hot and kept in a vacuum for 3 weeks. On scratching, a solid was obtained which, dissolved in alcohol and precipitated with ether, gave the *hydrochloride*. Crystallised from a very small quantity of alcohol, this formed slightly yellowish crystals (13 g.), m. p. 105° (Found : N, 4·45, 4·5. $C_{18}H_{21}O_3N$,HCl requires N, 4·7%).

1-*Di*-(β-*hydroxyethyl*)*amino*-5-(4′-*methoxyphenyl*)-Δ^4-*penten*-3-*one hydrochloride*, similarly prepared from diethanolamine hydrochloride, anisylideneacetone, and paraformaldehyde, formed squat, slightly yellow crystals, m. p. 84°, from *iso*propyl alcohol (Found : C, 58·3; H, 7·7. $C_{16}H_{23}O_4N$,HCl requires C, 58·3; H, 7·3%).

Di(*cinnamylethyl*)*piperazine Hydrochloride*.—Piperazine (4·3 g.) was dissolved in ethyl alcohol (20 ml.) and concentrated hydrochloric acid (8·9 ml.), and benzylideneacetone (14·6 g.) and paraformaldehyde (4·5 g. in 1·5 g. lots) added to the refluxing mixture. After 1½ hrs.' heating, the crystals that had separated were collected and washed with ethyl alcohol. They were soluble in hydrochloric acid (2N), slightly soluble in methyl alcohol containing some concentrated hydrochloric acid, and readily soluble in acetic acid, glacial or slightly diluted. Crystallised from aqueous acetic acid (1 : 1), the *compound* formed white needles which decomposed above 200° (Found : N, 5·8. $C_{26}H_{36}O_2N_2$,2HCl requires N, 5·9%).

The following new phenylhydrazones have been prepared by the method of Auwers and Voss (*loc. cit.*) : *Phenylhydrazone of* β-*dimethylaminopropiophenone hydrochloride*, yellow needles from ethyl alcohol, m. p. 172° (Found : C, 67·2; H, 7·25; N, 13·45. $C_{17}H_{21}N_3$,HCl requires C, 67·2; H, 7·25; N, 13·8%). *Phenylhydrazone of* β-*piperidylpropiophenone hydrochloride*, yellow plates from ethyl alcohol, m. p. 162° (Found : C, 69·5; H, 7·3; N, 12·1. $C_{20}H_{25}N_3$,HCl requires C, 69·9; H, 7·6; N, 12·2%). The *base*, precipitated by dilute alkali, crystallised from aqueous alcohol in pale yellow needles, m. p. 84° (Found : N, 13·7. $C_{20}H_{25}N_3$ requires N, 13·7%).

Preparation of 1 : 3-*Diphenylpyrazoline*.—By heating the phenylhydrazones of β-dimethylamino- and β-piperidylpropiophenone (in 1 g. quantities) with 50% acetic acid (10 ml.) and sodium acetate (1 g.) on a water-bath for 2 hrs., solids separated which, crystallised from ethyl alcohol, proved to be in each case 1 : 3-diphenylpyrazoline, m. p. and mixed m. p. with an authentic specimen 151°. The same compound was also obtained on heating dibenzoylethylpiperazine hydrochloride (2·1 g.) in 50% acetic acid (20 ml.) with sodium acetate (2 g.) and phenylhydrazine (2·2 g.) on a water-bath for 1½ hrs. The oily solid which separated solidified on cooling. Collected and washed with ethyl alcohol, this solid was boiled with 95% alcohol (150 ml.); most of it then dissolved, leaving a minute quantity of an unidentified white *compound*, m. p. 195° (Found : C, 76·8; H, 7·0%). The alcoholic solution, poured into water, gave 1 : 3-diphenylpyrazoline (mixed m. p. 151°).

Isomerisation of the Phenylhydrazones of α-*Unsaturated* β′-*Piperidinoethyl Ketone Hydrochlorides and Isolation of some* 3-*Vinylpyrazolines*.—The phenylhydrazones were refluxed with aqueous acetic acid (1 acid : 5 water) or hydrochloric acid (2N) until the normal isomerisation was complete, which generally occurred in a few minutes. In the cases indicated below, the reaction mixture on filtration left minute quantities of yellow solids, at present assigned the constitution of 3-vinylpyrazolines. The filtrates in most cases examined yielded the normal isomerisation products.

1-*Phenyl*-5-(3′ : 4′-*methylenedioxyphenyl*)-3-*vinylpyrazoline*. The phenylhydrazone of 1-piperidino-5-(3′ : 4′-methylenedioxyphenyl)-Δ^4-penten-3-one hydrochloride (4·4 g.), treated as described with aqueous acetic acid (15 ml.), gave a residue which crystallised from methyl alcohol in yellow plates (0·07 g.), m. p. 155° (Found : C, 73·7; H, 5·6. $C_{18}H_{16}O_2N_2$ requires C, 73·9; H, 5·5%). The filtrate contained 1-phenyl-3-(β-piperidylethyl)-5-(3′ : 4′-methylenedioxyphenyl)-pyrazoline hydrochloride.

1-Phenyl-5-(4'-methoxyphenyl)-3-vinylpyrazoline, similarly obtained from the phenylhydrazone of 1-piperidino-5-(4'-methoxyphenyl)-Δ^4-penten-3-one hydrochloride (12 g.), crystallised from 95% alcohol in yellow microcrystalline plates (0·01 g.), m. p. 180° (Found: C, 77·1; H, 6·8; N, 10·7. $C_{18}H_{18}ON_2$ requires C, 77·7; H, 6·4; N, 10·1%). The filtrate yielded the normal isomerisation product, 1-phenyl-3-(β-piperidylethyl)-5-(4'-methoxyphenyl)pyrazoline hydrochloride.

1 : 5-*Diphenyl-3-vinylpyrazoline*. This could not be isolated in the treatment of 1-piperidino-5-phenyl-Δ^4-penten-3-one hydrochloride with dilute acid. The crude phenylhydrazone obtained from 1-di-(β-hydroxyethyl)amino-5-phenyl-Δ^4-penten-3-one hydrochloride (36 g.), when heated with 2N-hydrochloric acid (150 ml.), gave a residue of the *vinylpyrazoline*. Crystallised from 95% alcohol, this formed bright yellow plates (1·7 g.), m. p. 138° (Found: C, 81·7; H, 6·2; N, 11·8. $C_{17}H_{16}N_2$ requires C, 82·2; H, 6·5; N, 11·3%).

The crude phenylhydrazone of dicinnamylethylpiperazine hydrochloride (4 g.), boiled under reflux with glacial acetic acid for 2 mins., gave a bright yellow solid which crystallised from 95% alcohol in plates (0·47 g.), m. p. 138°. This was proved by mixed m. p. to be identical with the compound described above (Found: C, 81·9; H, 6·4; N, 11·8%).

The author desires to thank the Governors of the Heriot Watt College for facilities and Mr. A. T. Macdonald for some micro-analyses.

HERIOT WATT COLLEGE, EDINBURGH. [*Received, September 7th*, 1944.]

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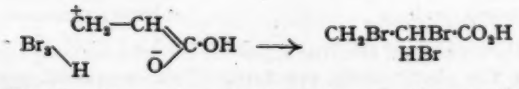
34. *The Kinetics of Halogen Addition to Unsaturated Compounds. Part V. The αβ-Unsaturated Acids and Hydrogen Bromide Catalysis.*

By I. D. MORTON and P. W. ROBERTSON.

ββ-Dimethylacrylic acid unites with bromine in acetic acid solution by a rapid termolecular reaction, which is only slightly accelerated by hydrogen bromide. Unsaturated acids in which electronic regression from the ethylene system is considerable show autocatalysed addition of bromine and are strongly catalysed by hydrogen bromide. These reactions by means of HBr_3 are nucleophilic, as the rates for related compounds, *e.g.*, acrylic and crotonic, maleic and citraconic, fumaric and mesaconic, glutaconic and β-methylglutaconic acids, are in the reverse order to the electrophilic rates of bromine addition in aqueous acetic acid. Benzylidenemalonic acid gives, relatively to cinnamic acid, a high rate of HBr_3 addition in acetic acid, and a low rate of bromine addition in aqueous acetic acid. Phenyl- and *n*-propyl-propiolic acids have also been investigated.

THE fact that αβ-olefinic acids may differ fundamentally with regard to addition of bromine in the presence of hydrogen bromide was pointed out in Part I (J., 1937, 335). It was found that addition of bromine to acrylic acid in acetic acid solution was strongly accelerated by hydrogen bromide, whereas *cis*-cinnamic acid under the same conditions showed no such catalysis. The acid-catalysed reaction with acrylic acid further differed from normal bromine addition in that its rate was decreased on addition of water to the solvent. Subsequently, Anantakrishnan and Venkataraman (J., 1939, 224) pointed out that crotonic and tiglic acids also showed marked catalysis by hydrogen bromide, and they proposed a chain mechanism involving the complex A, hydrogen bromide, and bromine activated by the acid. Nozaki and Ogg (*J. Amer. Chem. Soc.*, 1942, **68**, 697) have investigated hydrogen bromide and lithium bromide catalysed addition of bromine to maleic and fumaric acids in acetic acid solution, and conclude that these reactions proceed by a termolecular reaction between A, Br_2, and Br^-.

In this investigation a number of αβ-olefinic acids have been examined, and it appears that a theory of nucleophilic HBr_3 addition, with elimination of hydrogen bromide, offers a reasonable explanation of catalysis by the latter. There is an analogy with the αβ-olefinic aldehydes, which also show bromine addition strongly catalysed by the acid, but the change in rate of HBr_3 addition from the one type of compound to the other may be considerable; *e.g.*, crotonaldehyde reacts at 10^5 times the rate of crotonic acid, and this corresponds with the activity of these compounds to other nucleophilic reagents. With reference to the mechanism of the reaction, 1 : 4-addition of HBr_3, analogous to 1 : 4-addition of hydrogen cyanide to the corresponding aldehydes, is proposed to represent the initial stage. The reaction between acrylic acid and HBr_3 could therefore be formulated as



The attack is upon the positive β-carbon atom of the system, so the reaction is nucleophilic in type. The rates of related compounds should therefore decrease on replacing the hydrogen atoms of the β-carbon atom by electron-contributing groups, and consequently be in the reverse order of that found for electrophilic bromine addition. This is confirmed by the experimental results. If the relative rates of the HBr_3 reaction are taken as the difference between the rates of bromine addition with and without the same small amount of added hydrogen bromide, the order is $CH_2{:}CH{\cdot}CO_2H > CHMe{:}CH{\cdot}CO_2H > CMe_2{:}CH{\cdot}CO_2H$, and this is the reverse of the electrophilic rate of bromine addition in aqueous acetic acid (or of chlorine addition in acetic acid).

A further similarity between αβ-unsaturated acids and aldehydes is that bromine addition in acetic acid is accelerated by added acids, *e.g.*, sulphuric acid, whereas allyl compounds such as the benzoate show no such catalysis. The possibility that bromine can act under certain conditions as a nucleophilic reagent is being examined in an investigation on the αβ-unsaturated aldehydes.

The kinetics of bromine addition to an αβ-olefinic acid may vary with the nature of the compound and also,

for a given compound, with the concentration. In ββ-dimethylacrylic acid the inductive effect of the two methyl groups favours electrophilic addition, and the characteristic third-order reaction holds with small deviations over the concentration range investigated. Crotonic acid, in which electronic accession to the ethylenic system is less, reacts more slowly, adding bromine at an approximately third-order rate at the concentration region 0·1M; at lower concentrations the reaction merges into an autocatalysed reaction, with its disturbing effect on the reaction order. The following are the times for 10% reaction and reaction orders for bromine addition to ββ-dimethylacrylic acid in acetic acid at 24° :

	M/20.	M/40.	M/80.	M/160.
Time, mins., for $x = 10$	3·05	13·0	56·5	240
n	3·1	3·1	3·1	

The kinetics of the hydrogen bromide-catalysed reactions in acetic acid are complex, and the interpretation uncertain, for the reaction $HBr + Br_2 \rightleftharpoons HBr_3$ appears to show a variation in K with the concentration (Jones, J., 1911, **99**, 402). The rates for ββ-dimethylacrylic and crotonic acids with various amounts of hydrogen bromide show the characteristic differences between these two types of compound. For M/80-acid in acetic acid at 24° :

[HBr]/[Br_2].	0·0.	0·25.	0·5.	1.	2.	4.
$CMe_2{:}CH{\cdot}CO_2H$, k_2 ($x = 10$)	0·15	0·15	0·16	0·18	0·18	0·18
$CHMe{:}CH{\cdot}CO_2H$, k_2 ($x = 10$)	<0·006	0·018	0·030	0·051	0·051	0·051

ββ-Dimethylacrylic acid, which has a high electrophilic rate for bromine addition, differs from crotonic and acrylic acids in that the rate is only slightly accelerated by hydrogen bromide. Values with allyl compounds (Part VI, following paper) indicate that HBr_3 may act as an electrophilic reagent. This also appears probable from a consideration of the following relative rates.

Bimolecular coefficients in acetic acid at 24°.

	$CMe_2{:}CH{\cdot}CO_2H$.	$CHMe{:}CH{\cdot}CO_2H$.	$CH_2{:}CH{\cdot}CO_2H$.
k_2 (Cl_2)	51	0·62	0·017
k_2 (HBr_3)	0·18	0·051	0·42

Addition of chlorine is in the normal electrophilic order; that of HBr_3 is in the nucleophilic order for acrylic and crotonic acids, but for dimethylacrylic acid there is a reversal in rate. The conclusion is that the mechanism changes in this series, and the high rate for dimethylacrylic acid with HBr_3 is due to electrophilic addition.

The dicarboxylic unsaturated acids show marked catalysis by hydrogen bromide of bromine addition. The values in the presence of the bromide are shown in the following table as bimolecular rates for $x = 10$ and M/80-solutions at 24°.

[HBr]/[Br_2].	1.	4.	[HBr]/[Br_2].	1.	4.
Maleic acid	0·27	0·56	Glutaconic acid	0·090	0·44
Fumaric acid	0·019	0·047	β-Methylglutaconic acid	0·015	0·049
Citraconic acid	0·0054	0·012	Benzylidenemalonic acid	26	26
Mesaconic acid	0·014	0·025			

In HBr_3 addition a nucleophilic mechanism operates, for the rates for related compounds are in the reverse order to the velocities of bromine addition in aqueous acetic acid, *i.e.*, under conditions favourable for the electrophilic reaction. This is evident from the following comparison, for which the rates with 4 mols. of hydrogen bromide are taken as a relative measure of HBr_3 addition.

Relative rates of nucleophilic and electrophilic addition.

HBr_3 in HOAc.	Br_2 in HOAc (25%) + H_2O (75%).
Maleic : Citraconic = 45 : 1	Citraconic : Maleic = 15 : 1
Fumaric : Mesaconic = 2 : 1	Mesaconic : Fumaric = 15 : 1
Glutaconic : β-Methylglutaconic = 9 : 1	β-Methylglutaconic : Glutaconic = 45 : 1

In benzylidenemalonic acid the combined electronic pull of the two carboxyl groups favours the nucleophilic reaction and is unfavourable to the electrophilic reaction. This compound gives in acetic acid a high rate with HBr_3, about 40 times as rapid as cinnamic acid, whereas its electrophilic rate of bromine addition in 25% aqueous acetic acid is low, being about 100 times slower than that of cinnamic acid.

Phenylpropiolic acid in acetic acid solution at 24° shows third-order kinetics :

	M/10.	M/20.	M/40.	M/80.
Time, mins., for $x = 20$	55	240	980	3750
n	3·1	3·0	2·9	

At each concentration the termolecular coefficients remain constant over the first 60% of the reaction :

x	10	20	30	40	50	60
k_3 (M/40)	1·9	1·9	1·9	1·9	2·0	2·0

As hydrogen bromide is a catalyst, this constancy indicates it is not formed during the reaction, and this

was confirmed by testing the reaction mixture. The catalytic effect of hydrogen bromide is shown by the following initial rates in acetic acid at 24°, calculated as bimolecular coefficients;

$[HBr]/Br_2$	0	0·25	0·5	1	4	6
k_2, M/80 ($x = 10$)	0·0053	0·012	0·018	0·030	0·032	0·032

With addition of water to the acetic acid, the rate of bromine addition increases in the manner characteristic of the electrophilic addition, and the reaction becomes bimolecular.

n-Propylpropiolic acid adds bromine rapidly, the initial rate at M/20 being 300 times that of phenylpropiolic acid, but this falls off considerably on reducing the concentration; in acetic acid at 24° :

	M/20.	M/40.	M/80.
Time, mins. ($x = 5$)	0·35	2·5	100

At each concentration there is a deceleration as the reaction proceeds, becoming more pronounced at lower concentrations, and less than 1 mol. of bromine reacts with 1 mol. of the propylpropiolic acid. These results are interpreted as indicating a chain mechanism, with partial polymerisation to less unsaturated products. Addition of water to the solvent reduces the rate and makes the reaction proceed normally.

This investigation provides data for the comparison of the velocity of bromine addition to related olefinic and acetylenic compounds :

	cis-CHPh:CH·CO_2H.	CPh:C·CO_2H.
k_2 (HOAc), 24°	21	2·0
	trans-CHMe:CH·CO_2Me.*	CEt:C·CO_2Me.
k_2 (50% H_2O/HOAc), 24°	2·4	0·035

* Methyl- and ethyl-acrylic acids have approximately the same rate of bromine addition in carbon tetrachloride solution (Sudborough and Thomas, J., 1910, **97**, 719).

It is apparent that acetylenic compounds add halogen by the electrophilic mechanism less rapidly than the corresponding olefinic compounds. This effect appears to be general and is being further investigated.

Experimental.

The technique is as previously described. The following compounds were used: crotonic acid, m. p. 71·5°; ββ-dimethylacrylic acid, m. p. 70°; maleic acid, m. p. 128·5°; fumaric acid, m. p. 285°; citraconic acid, m. p. 90°; glutaconic acid, m. p. 135°; β-methylglutaconic acid, m. p. 147°; phenylpropiolic acid, m. p. 146°; *n*-propylpropiolic acid, m. p. 24°; methyl ethylpropiolate, b. p. 47°/10 mm. We are indebted to Professor J. Packer, Christchurch, N.Z., for the specimens of glutaconic acids, and to Dr. G. F. Henion, Notre Dame, Indiana, for the alkylpropiolic acid compounds.

Details of a typical experiment are:

M/20-Dimethylacrylic acid and M/20-bromine in acetic acid at 24°.

Reaction mixture, 10 ml.; 1-ml. samples titrated with 0·05N-$Na_2S_2O_3$.

Time, mins.	0	1·95	3·95	5·90	8·65
Titre, ml.	2·00	1·88	1·72	1·64	1·49

From curve : $x = 10$, $t = 3·0$; $x = 20$, $t = 6·6$. Second expt. : $x = 10$, $t = 3·1$; $x = 20$, $t = 6·8$.

The times for this compound at other concentrations have been given on p. 130.

For experiments with added hydrogen bromide, portions of a concentrated solution of hydrogen bromide (standardised at intervals) were added. The times for 4 mols. of hydrogen bromide have been given; those for $x = 10$ for M/80-acid and M/80-bromine in acetic acid at 24° are : ββ-dimethylacrylic, $t = 50$; crotonic, $t = 175$; maleic, $t = 15$; fumaric, $t = 190$; citraconic, $t = 700$; mesaconic, $t = 350$; glutaconic, $t = 20$; β-methylglutaconic, $t = 180$; benzylidenemalonic, $t = 0·48$.

Reactions with sulphuric acid showed the following ratios to uncatalysed reactions. For M/80-crotonic acid + M/80-bromine : $[H_2SO_4]$, 1·5; $4[H_2SO_4]$, 3·1. For M/80-allyl benzoate + M/80-bromine : $2[H_2SO_4]$, 1·0.

The times in aqueous acetic acid (25% acid) at 24° were as follows (M/80-reactants, $x = 10$) : maleic, $t = 36$; fumaric, $t = 80$; citraconic, $t = 2·3$; mesaconic, $t = 6·4$; glutaconic, $t\ (x = 50) = 13·7$; β-methylglutaconic, $t\ (x = 50) = 0·30$; benzylidenemalonic (in 75% acid), $t\ (x = 10) = 8·5$.

Our thanks are due to Mr. D. H. Freeman for the preparation of phenylpropiolic acid and measurements with this compound, and to Mr. P. B. D. de la Mare for assistance with certain of the measurements.

Victoria University College, Wellington, N.Z. [*Received, November 17th*, 1944.]

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35. *The Kinetics of Halogen Addition to Unsaturated Compounds. Part VI. The Allyl Halides : Lithium Chloride and Hydrogen Bromide Catalysis.*

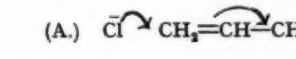
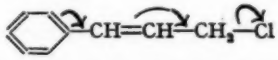
By B. E. Swedlund and P. W. Robertson.

Allyl chloride and bromide add bromine in acetic acid solution at a slower rate than allyl benzoate, and their reactions are accelerated by hydrogen bromide and considerably so by lithium chloride. These anomalies are not shown by γ-phenylallyl chloride and allyl benzoate. A theory, involving nucleophilic attack on the γ-carbon atom of the system, is proposed. Evidence is also produced to show that HBr_3 addition, when there is considerable electron accession to the ethylenic system, may take place by an electrophilic mechanism.

ALLYL chloride and bromide differ in certain respects from related compounds in their mode of bromine addition. Nozaki and Ogg (*J. Amer. Chem. Soc.*, 1942, **68**, 709) showed that addition of bromine to the former in acetic acid solution is much accelerated by lithium chloride, and implied that such behaviour is typical. They accordingly formulated a general mechanism for bromine addition, involving the simultaneous attack by an ion (OAc^-, Cl^-, or Br^-) and the bromine molecule. The normal influence of lithium chloride in electrophilic addition of bromine in acetic acid solution appears to be a small acceleration. As acetic acid has a low dielectric constant, and lithium chloride acts as a strong electrolyte in this solvent, a salt effect is possible, and this has been proposed to explain the similar relatively small acceleration observed by us for bromine and chlorine substitution (J., 1943, 279). On the other hand, lithium chloride considerably accelerates bromine addition to allyl chloride and bromide. The ratios of the rates of catalysed reactions for M/80-acid + M/80-bromine + M/20-lithium chloride to the uncatalysed reactions in acetic acid at 24° are :

$CH_2{:}CH{\cdot}CH_2Br$	$CH_2{:}CH{\cdot}CH_2Cl$	$CHPh{:}CH{\cdot}CH_2Cl$	$CH_2{:}CH{\cdot}CH_2{\cdot}OBz$
5·5	6·3	1·3	1·9

The accelerations with allyl bromide and allyl chloride are so considerable that a change in mechanism is indicated, and correspondingly there is a change, as determined from the initial rates at different concentrations, with respect to A + Br_2 (where A = the acid), from third-order towards second-order kinetics. Especially significant is the difference between allyl chloride and its γ-phenyl derivative. An attack by the chloride ion

(A.)  (B.) 

on allyl chloride (cf. Hughes, *Trans. Faraday Soc.*, 1941, **37**, 630) may be represented by (A). The ion thus formed, owing to its negative charge, would be susceptible to electrophilic attack by bromine. With (B), on the other hand, tautomeric displacement through the phenyl group reduces the positive charge on the γ-carbon atom, and so lessens the attack by chloride ions. Consequently, the mechanism for the action of bromine on allyl chloride in the presence of lithium chloride could be expressed by

$$A + Cl^- \rightleftarrows \bar{A}Cl \xrightarrow{Br_2} AClBr + Br^-$$

Nozaki and Ogg (*loc. cit.*) find that hydrogen bromide accelerates bromine addition to allyl chloride in acetic acid solution, and they regard this as the normal behaviour. Some compounds, however, may show the reverse effect, as is illustrated by the following ratios of velocities for M/80-reactants plus M/20-hydrogen bromide to the uncatalysed reactions in acetic acid at 24° :

$CH_2{:}CH{\cdot}CH_2Br$	$CH_2{:}CH{\cdot}CH_2Cl$	$CHPh{:}CH{\cdot}CH_2Cl$	$CH_2{:}CH{\cdot}CH_2{\cdot}OBz$
2·1	2·3	0·27	0·67

These reactions were further examined with different amounts of hydrogen bromide, and these results are shown as bimolecular coefficients :

$[HBr]/[Br_2]$.	0.	1.	4.	8.	16.
(I) $CH_2{:}CH{\cdot}CH_2Cl$, k_2 ($x = 20$)	1·6	3·6	3·8	3·8	—
(II) $CH_2{:}CH{\cdot}CH_2Br$, k_2 ($x = 20$)	1·0	—	2·2	2·2	—
(III) $CH_2{:}CH{\cdot}CH_2{\cdot}OBz$, k_2 ($x = 20$)	13·8	13·5	9·2	8·5	8·3
(IV) $CHPh{:}CH{\cdot}CH_2Cl$, k_2 ($x = 50$)	58	—	16	14	—

As the rates become constant with increasing amounts of hydrogen bromide, it is concluded that the catalysed reactions take place by HBr_2 addition. It is apparent that the reactions of compounds (I) and (II), which show considerable catalysis by lithium chloride, are accelerated by hydrogen bromide, and the reverse is true for (III) and (IV), the reactions of which are not considerably catalysed by lithium chloride. For (I) and (II), this is regarded as indicating a nucleophilic attack by HBr_2. The theoretical rates of nucleophilic addition are (I) > (II) > (III). There thus appears to be a change in mechanism in the series, and HBr_2 addition to allyl benzoate is therefore considered to be electrophilic in character (as for ββ-dimethylacrylic acid, Part V). Similarly, the nucleophilic rates should be (I) > (IV), and the reverse effect is explained if HBr_2 addition to phenylallyl chloride proceeded by an electrophilic mechanism. With regard to (I), although the nucleophilic mode of reaction appears to be dominant, it is reasonable to assume, by comparison with (III), that it is accompanied by a certain amount of simultaneous electrophilic HBr_2 addition. With reference to this dual mechanism, allyl chloride shows in its reactivity an analogy with benzyl chloride, which for similar reasons, *viz.*, the electron-repelling and electron-attracting power of the CH_2Cl group, undergoes *op*- as well as *m*-substitution.

The expected electrophilic order for the relative velocities of uncatalysed bromine addition to allyl compounds in acetic acid is benzoate ≫ bromide > chloride, whereas the experimental result is benzoate ≫ chloride > bromide. Bromine addition to allyl bromide and allyl chloride, owing to hydrogen bromide formed in the reaction by the partial addition of acetate ions in the process, is autocatalytic. This autocatalysis is more pronounced for allyl chloride than the bromide, and thus tends to reverse the relative order of these two compounds; but this alone does not seem sufficient to cause the reversal in rate. There is the further possibility that the velocities of these two compounds are determined in part by a nucleophilic attack by the solvent. In this connection, it is significant that the order remains unaltered for the bimolecular bromine addition in aqueous

acetic acid. In carbon tetrachloride there is the normal electrophilic order, as is seen from the initial rates (l.g.-mol.$^{-1}$, min.$^{-1}$) at 15° : allyl bromide, k_2 ($x = 20$), 0·030; allyl chloride, k_2 ($x = 20$), 0·017 (Juvala, *Ber.*, 1930, **63**, 1998).

Experimental.

The compounds used were allyl bromide, b.p. 67—68°/754 mm.; allyl chloride, b.p. 44·0—44·5°/744 mm.; γ-phenylallyl chloride, b.p. 122°/18 mm. Owing to their sensitivity to light, allyl chloride and bromide were weighed in a dim light. The solutions in acetic acid were stable, showing identical rates when freshly prepared and after being kept. The semi-micro technique was employed, and reactions were carried out in the dark. Data for a typical experiment were :

M/50-*Allyl chloride* + M/50-*bromine in acetic acid at* 24°.

Reaction mixture, 10 ml.; 2-ml. samples titrated with 0·02N-$Na_2S_2O_3$.

Time, mins.	0	1·6	4·4	8·0
Titre, ml.	3·97	3·67	3·23	2·64

From curve : at $x = 20\%$, $t = 4·7$; second expt., $x = 20\%$, $t = 4·8$.

Other results for allyl chloride in acetic acid at 25° are : times (mins.) for $x = 20$: reactants 0·04M, $t = 1·06$; 0·0125M, $t = 12·7$; 0·0125M + 0·05M-HCl, $t = 10·2$; 0·0125M + 0·05M-H_2SO_4, $t = 8·4$; 0·0125M + 0·05M-HBr, $t = 5·3$; 0·0125M + 0·05M-LiCl, $t = 2·0$.

The order for the reaction between allyl chloride and bromine (0·04—0·02M) was $n = 3·2$, somewhat higher than the values, 3·0—3·1, obtained for other compounds over this concentration range. This higher value is possibly to be attributed to the disturbing effect of hydrogen bromide catalysis. Nozaki and Ogg (*loc. cit.*, Table II) give rates that show for the same range $n = 3·7$, whereas the rates (Tables III and IV) show $n = 3·3$. Since the reaction is autocatalytic, owing to hydrogen bromide formation, it is necessary to evaluate n for the same initial percentage change. As a result of this autocatalysis the reaction shows rising bimolecular coefficients : M/80-allyl chloride + M/80-bromine, k_2 ($x = 10$) 1·5; k_2 ($x = 50$) 1·8. Nozaki and Ogg (Table I) show for the same reaction at 0·008M, constant bimolecular coefficients (*ca.* 0·020, with seconds as the time unit), whereas the conventional method of calculation (times from $x = 0$) gives from the smoothed curve k_2 ($x = 20$), 0·026; k_2 ($x = 60$), 0·050.

Allyl bromide + bromine ($x = 20$) : 0·04M, $t = 1·48$; 0·02M, $t = 6·6$; 0·0125M, $t = 19·3$; 0·0125M + 0·05M-HBr, $t = 9·2$; 0·0125M + 0·1M-LiCl, $t = 1·75$.

γ-Phenylallyl chloride + bromine ($x = 50$) : 0·0125M, $t = 1·39$; 0·125M + 0·05M-HBr, $t = 4·9$; 0·0125M + 0·1M-HBr, $t = 5·6$; 0·0125M + 0·05M-LiCl, $t = 1·0$; 0·0125M + 0·05M-HCl, $t = 1·37$.

Allyl benzoate + bromine ($x = 20$) : 0·0125M, $t = 1·45$; 0·0125M + 0·05M-HBr, $t = 2·13$; 0·0125M + 0·1M-HBr, $t = 2·30$; 0·0125M + 0·2M-HBr, $t = 2·27$. In these experiments fission of hydrogen bromide is excluded, as the same rates were found immediately on adding hydrogen bromide to the allyl benzoate in acetic acid, and on keeping the solutions.

Victoria University College, Wellington, N.Z.

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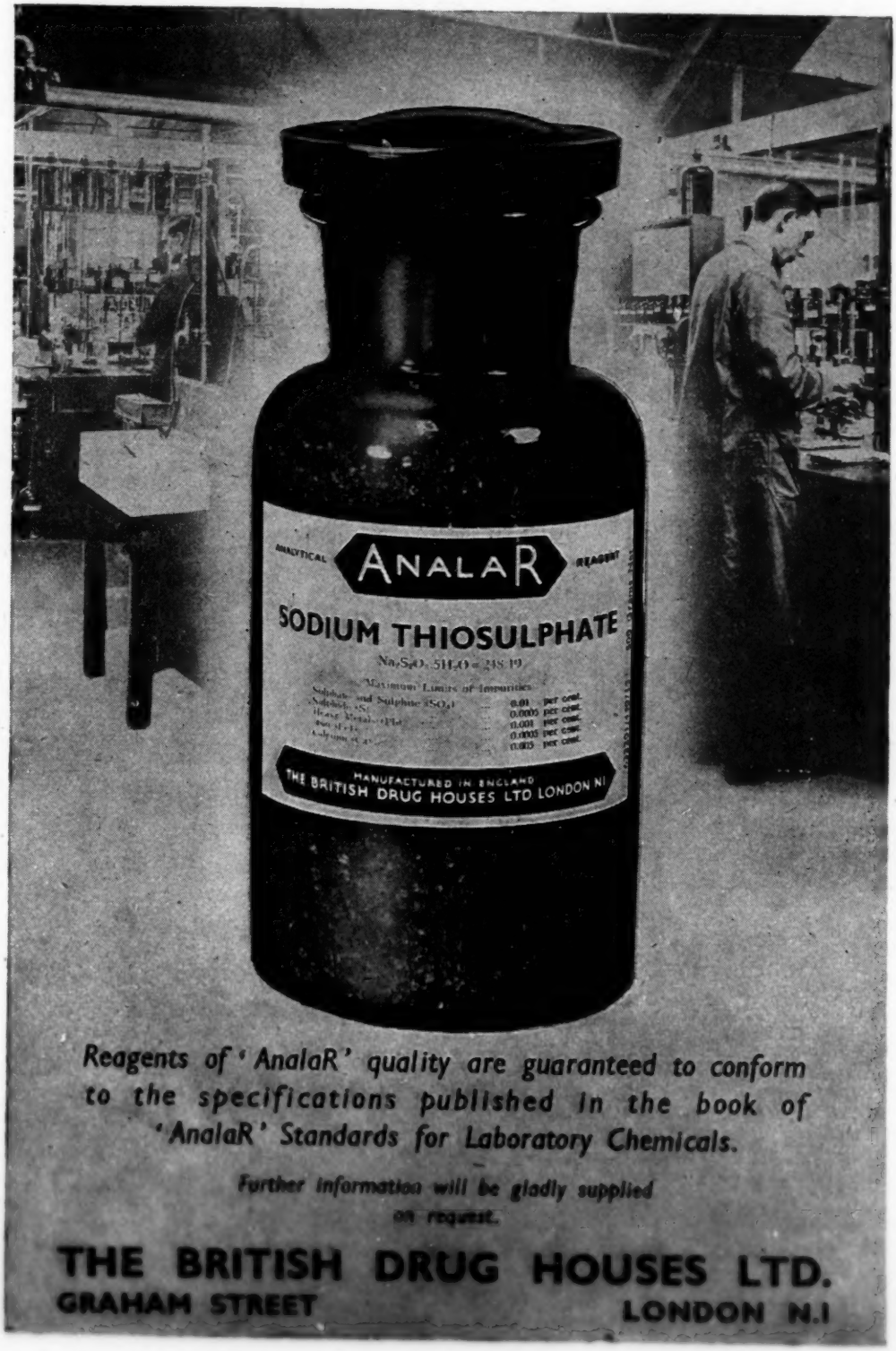
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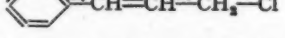
ALLYL chloride and bromide differ in certain respects from related compounds in their mode of bromine addition. Nozaki and Ogg (*J. Amer. Chem. Soc.*, **1942**, **68**, 709) showed that addition of bromine to the former in acetic acid solution is much accelerated by lithium chloride, and implied that such behaviour is typical. They accordingly formulated a general mechanism for bromine addition, involving the simultaneous attack by an ion (OAc^-, Cl^-, or Br^-) and the bromine molecule. The normal influence of lithium chloride in electrophilic addition of bromine in acetic acid solution appears to be a small acceleration. As acetic acid has a low dielectric constant, and lithium chloride acts as a strong electrolyte in this solvent, a salt effect is possible, and this has been proposed to explain the similar relatively small acceleration observed by us for bromine and chlorine substitution (J., **1943**, 279). On the other hand, lithium chloride considerably accelerates bromine addition to allyl chloride and bromide. The ratios of the rates of catalysed reactions for M/80-acid + M/80-bromine + M/20-lithium chloride to the uncatalysed reactions in acetic acid at 24° are :

$CH_2{:}CH{\cdot}CH_2Br$	$CH_2{:}CH{\cdot}CH_2Cl$	$CHPh{:}CH{\cdot}CH_2Cl$	$CH_2{:}CH{\cdot}CH_2{\cdot}OBz$
5·5	6·3	1·3	1·9

The accelerations with allyl bromide and allyl chloride are so considerable that a change in mechanism is indicated, and correspondingly there is a change, as determined from the initial rates at different concentrations, with respect to A + Br_2 (where A = the acid), from third-order towards second-order kinetics. Especially significant is the difference between allyl chloride and its γ-phenyl derivative. An attack by the chloride ion

(A.) $\bar{Cl}\curvearrowright CH_2{=}CH{-}CH_2{-}Cl$ (B.) 

on allyl chloride (cf. Hughes, *Trans. Faraday Soc.*, **1941**, **37**, 630) may be represented by (A). The ion thus formed, owing to its negative charge, would be susceptible to electrophilic attack by bromine. With (B), on the other hand, tautomeric displacement through the phenyl group reduces the positive charge on the γ-carbon atom, and so lessens the attack by chloride ions. Consequently, the mechanism for the action of bromine on allyl chloride in the presence of lithium chloride could be expressed by

$$A + Cl^- \rightleftarrows \bar{A}Cl \xrightarrow{Br_2} AClBr + Br^-$$

Nozaki and Ogg (*loc. cit.*) find that hydrogen bromide accelerates bromine addition to allyl chloride in acetic acid solution, and they regard this as the normal behaviour. Some compounds, however, may show the reverse effect, as is illustrated by the following ratios of velocities for M/80-reactants plus M/20-hydrogen bromide to the uncatalysed reactions in acetic acid at 24° :

$CH_2{:}CH{\cdot}CH_2Br$	$CH_2{:}CH{\cdot}CH_2Cl$	$CHPh{:}CH{\cdot}CH_2Cl$	$CH_2{:}CH{\cdot}CH_2{\cdot}OBz$
2·1	2·3	0·27	0·67

These reactions were further examined with different amounts of hydrogen bromide, and these results are shown as bimolecular coefficients :

$[HBr]/[Br_2]$.	0.	1.	4.	8.	16.
(I) $CH_2{:}CH{\cdot}CH_2Cl$, k_2 ($x = 20$)	1·6	3·6	3·8	3·8	—
(II) $CH_2{:}CH{\cdot}CH_2Br$, k_2 ($x = 20$)	1·0	—	2·2	2·2	—
(III) $CH_2{:}CH{\cdot}CH_2{\cdot}OBz$, k_2 ($x = 20$)	13·8	13·5	9·2	8·5	8·3
(IV) $CHPh{:}CH{\cdot}CH_2Cl$, k_2 ($x = 50$)	58	—	16	14	—

As the rates become constant with increasing amounts of hydrogen bromide, it is concluded that the catalysed reactions take place by HBr_2 addition. It is apparent that the reactions of compounds (I) and (II), which show considerable catalysis by lithium chloride, are accelerated by hydrogen bromide, and the reverse is true for (III) and (IV), the reactions of which are not considerably catalysed by lithium chloride. For (I) and (II), this is regarded as indicating a nucleophilic attack by HBr_2. The theoretical rates of nucleophilic addition are (I) > (II) > (III). There thus appears to be a change in mechanism in the series, and HBr_2 addition to allyl benzoate is therefore considered to be electrophilic in character (as for ββ-dimethylacrylic acid, Part V). Similarly, the nucleophilic rates should be (I) > (IV), and the reverse effect is explained if HBr_2 addition to phenylallyl chloride proceeded by an electrophilic mechanism. With regard to (I), although the nucleophilic mode of reaction appears to be dominant, it is reasonable to assume, by comparison with (III), that it is accompanied by a certain amount of simultaneous electrophilic HBr_2 addition. With reference to this dual mechanism, allyl chloride shows in its reactivity an analogy with benzyl chloride, which for similar reasons, *viz.*, the electron-repelling and electron-attracting power of the CH_2Cl group, undergoes *op*- as well as *m*-substitution.

The expected electrophilic order for the relative velocities of uncatalysed bromine addition to allyl compounds in acetic acid is benzoate ≫ bromide > chloride, whereas the experimental result is benzoate ≫ chloride > bromide. Bromine addition to allyl bromide and allyl chloride, owing to hydrogen bromide formed in the reaction by the partial addition of acetate ions in the process, is autocatalytic. This autocatalysis is more pronounced for allyl chloride than the bromide, and thus tends to reverse the relative order of these two compounds; but this alone does not seem sufficient to cause the reversal in rate. There is the further possibility that the velocities of these two compounds are determined in part by a nucleophilic attack by the solvent. In this connection, it is significant that the order remains unaltered for the bimolecular bromine addition in aqueous

acetic acid. In carbon tetrachloride there is the normal electrophilic order, as is seen from the initial rates (l.g.-mol.$^{-1}$, min.$^{-1}$) at 15° : allyl bromide, k_2 ($x = 20$), 0·030; allyl chloride, k_2 ($x = 20$), 0·017 (Juvala, *Ber.*, 1930, **63**, 1998).

Experimental.

The compounds used were allyl bromide, b.p. 67—68°/754 mm.; allyl chloride, b.p. 44·0—44·5°/744 mm.; γ-phenylallyl chloride, b.p. 122°/18 mm. Owing to their sensitivity to light, allyl chloride and bromide were weighed in a dim light. The solutions in acetic acid were stable, showing identical rates when freshly prepared and after being kept. The semi-micro technique was employed, and reactions were carried out in the dark. Data for a typical experiment were :

M/50-Allyl chloride + M/50-bromine in acetic acid at 24°.

Reaction mixture, 10 ml.; 2-ml. samples titrated with 0·02N-$Na_2S_2O_3$.

Time, mins.	0	1·6	4·4	8·0
Titre, ml.	3·97	3·67	3·23	2·64

From curve : at $x = 20\%$, $t = 4·7$; second expt., $x = 20\%$, $t = 4·8$.

Other results for allyl chloride in acetic acid at 25° are : times (mins.) for $x = 20$: reactants 0·04M, $t = 1·06$; 0·0125M, $t = 12·7$; 0·0125M + 0·05M-HCl, $t = 10·2$; 0·0125M + 0·05M-H_2SO_4, $t = 8·4$; 0·0125M + 0·05M-HBr, $t = 5·3$; 0·0125M + 0·05M-LiCl, $t = 2·0$.

The order for the reaction between allyl chloride and bromine (0·04—0·02M) was $n = 3·2$, somewhat higher than the values, 3·0—3·1, obtained for other compounds over this concentration range. This higher value is possibly to be attributed to the disturbing effect of hydrogen bromide catalysis. Nozaki and Ogg (*loc. cit.*, Table II) give rates that show for the same range $n = 3·7$, whereas the rates (Tables III and IV) show $n = 3·3$. Since the reaction is autocatalytic, owing to hydrogen bromide formation, it is necessary to evaluate n for the same initial percentage change. As a result of this autocatalysis the reaction shows rising bimolecular coefficients : M/80-allyl chloride + M/80-bromine, k_2 ($x = 10$) 1·5; k_2 ($x = 50$) 1·8. Nozaki and Ogg (Table I) show for the same reaction at 0·008M, constant bimolecular coefficients (*ca.* 0·020, with seconds as the time unit), whereas the conventional method of calculation (times from $x = 0$) gives from the smoothed curve k_2 ($x = 20$), 0·026; k_2 ($x = 60$), 0·050.

Allyl bromide + bromine ($x = 20$) : 0·04M, $t = 1·48$; 0·02M, $t = 6·6$; 0·0125M, $t = 19·3$; 0·0125M + 0·05M-HBr, $t = 9·2$; 0·0125M + 0·1M-LiCl, $t = 1·75$.

γ-Phenylallyl chloride + bromine ($x = 50$) : 0·0125M, $t = 1·39$; 0·125M + 0·05M-HBr, $t = 4·9$; 0·0125M + 0·1M-HBr, $t = 5·6$; 0·0125M + 0·05M-LiCl, $t = 1·0$; 0·0125M + 0·05M-HCl, $t = 1·37$.

Allyl benzoate + bromine ($x = 20$) : 0·0125M, $t = 1·45$; 0·0125M + 0·05M-HBr, $t = 2·13$; 0·0125M + 0·1M-HBr, $t = 2·30$; 0·0125M + 0·2M-HBr, $t = 2·27$. In these experiments fission of hydrogen bromide is excluded, as the same rates were found immediately on adding hydrogen bromide to the allyl benzoate in acetic acid, and on keeping the solutions.

Victoria University College, Wellington, N.Z.

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36. *The Metal-catalysed Reaction between Acetylene and Hydrogen. Part II. Further Experiments with Nickel Catalysts.*

By J. Sheridan.

The effect of temperature on the reaction between acetylene and hydrogen over a nickel–pumice catalyst has been systematically studied in the range 0—126°. Lowering the temperature increases the production of ethylene and (more markedly) ethane; the yield of C_2 hydrocarbons, in terms of the acetylene not recovered, is 31% at 126° and 65% at 0—3° for 1 : 1 gas mixtures. The ratio of the acetylene removed as other products to the hydrogen so removed increases as the temperature is raised.

Temperature (0—91°) has little influence on the orders of the reactions occurring.

With some not improbable assumptions, activation energies, uncorrected for desorption of gas, are deduced as follows :

(I) $C_2H_2 + H_2 + Ni \longrightarrow C_2H_4 + Ni$: 10·9 kg.-cals. at 0—126°

(II) $C_2H_2 + xH_2 + Ni \longrightarrow$ products other than C_2 hydrocarbons + Ni : 14·5 kg.-cals. at 0°, falling to 12·7 kg.-cals. at 126°.

The products higher than the C_2 series from 1 : 1 gas mixtures at 200—250° over nickel–pumice cover a wide range of molecular weights. The chief constituents of the fully hydrogenated products boiling below 70° are *n*-hexane, 3-methylpentane, and probably *n*-butane, *i.e.*, those substances the carbon skeletons of which can be formed by linking together C–C units. In addition, *n*-pentane, 2-methylbutane, 2-methylpentane, 3-methylhexane, and probably *n*-heptane are present, as well as octanes and higher hydrocarbons, in the hydrogenated products.

The mechanisms of the reactions are discussed, and it is suggested that reaction (II) is a surface chain reaction, initiated through a half-hydrogenated state in associatively chemisorbed acetylene.

The effect of temperature on the nickel-catalysed reaction between acetylene and hydrogen has not hitherto been systematically investigated, though there are qualitative indications that an increase in temperature decreases the yields of C_2 hydrocarbons (*e.g.*, Sabatier and Senderens, *Compt. rend.*, 1899, **128**, 1173). A systematic study of the influence of temperature on the rate and products of the reaction is now reported.

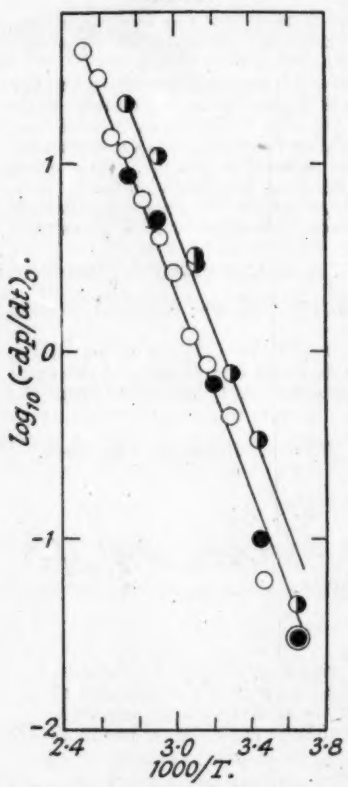
The products other than C_2 hydrocarbons over nickel are known to consist mainly of aliphatic hydrocarbons of various degrees of saturation, covering a wide range of molecular weights (see references in Part I, J., 1944, 373). With nickel–pumice, production of C_4 hydrocarbons has been reported to be slightly favoured (Petrov and Antsus, *Compt. rend. Acad. Sci. U.R.S.S.*, 1934, **4**, 300; *J. Appl. Chem. U.S.S.R.*, 1933, **6**, 1145), but

there is little doubt that C_8 derivatives and numerous higher hydrocarbons are formed, and probably also C_4 compounds (cf. Dupont and Lombard, *Bull. Soc. chim.*, 1941, **8**, 851). Oxidation studies (Petrov and Antsus, *loc. cit.*, 1934) give some support for the presence of branched olefins. The available data do not exclude the possibility of minor quantities of derivatives of pentanes, heptanes, etc., being present.

Careful study of individual products has unfortunately only been made in the case of nickel on a highly active base, zinc chloride. With this type of catalyst, Petrov and Antsus (*J. Physical Chem., U.S.S.R.*, 1940, **14**, 1308; *Bull. Acad. Sci. U.R.S.S., Classe sci. chim.*, 1940, 274; cf. Russian Patent, 1940, 58,320) report butadiene and especially *iso*butene. Since the work now described was done, evidence has become available (*idem, ibid.*, 1942, p. 125) that the higher fractions over the same type of catalyst contain various mono- and di-olefins with the carbon skeletons of *n*-hexane, 2- and 3-methylpentanes, 2 : 3-dimethylbutane, 3-ethylhexane, and 2-, 3-, and 4-methylheptanes. Traces of benzene were found, and *n*-C_8 hydrocarbons were also considered present. Considerably more *n*-hexane derivatives were formed than any other single type of structure, though both methylpentane skeletons were common. The formation of *n*- and *iso*-butene structures over nickel on a less active base, kaolin, is also mentioned by Antsus and Petrov (*loc. cit.*, 1942), and apparently part of the product examined for C_6 and C_8 compounds was prepared over nickel alone, but scarcely any details are given of the conditions of preparation.

More knowledge is required of the yields and structures of individual products over nickel on a base less reactive than zinc chloride, and an account is given below of a study of the products obtained over a nickel-pumice catalyst similar to those used in Part I (*loc. cit.*).

FIG. 1.



Open circles: 197—202 *mm.* H_2, 197—202 *mm.* C_2H_2.
Full circles: 199—201 *mm.* H_2, 400—403 *mm.* C_2H_2.
Half-filled circles: 399—403 *mm.* H_2, 199—202 *mm.* C_2H_2.

EXPERIMENTAL.

Effect of Temperature on Reaction.—The materials and method were as described in Part I. The nickel–pumice catalyst was a specimen of Ni-2 (nickel : pumice ratio 1 : 5). Temperature control was somewhat less accurate below 20° than at higher temperatures, variations within a range of 2—3° being recorded. Manometer readings were corrected to a constant temperature for each run, and for any changes in barometric pressure. In the fastest reaction (at 126°) time did not permit a preliminary washing of the capillary leads from the reaction bulb before collection of the gas.

The experiments were performed in a sequence unrelated to the variations in conditions, and the satisfactory constancy of the activity of the catalyst (see Part I) is confirmed by the mutually consistent results. The systematic variations in the rate and products of reaction must be an effect of the change in temperature.

Preparation of Hydrocarbon Products higher than the C_2 Series.—The nickel-pumice catalyst was prepared in the same way as Ni-2 (Part I), except that the final reduction was performed in hydrogen at 300° for 12 hours. A 20-cm. layer of this catalyst was placed in the electrically heated Pyrex reaction tube (15 mm. diam.). Acetylene (cylinder gas, passed through 2 wash-bottles of sodium bisulphite solution and through 20% sodium hydroxide) and hydrogen (electrolytic cylinder gas, 99·5% pure with traces of carbon monoxide and dioxide) were passed in at approximately equal rates (total rate 10—20 l./hr.), the combined gases being dried before reaction in a U-tube of anhydrous calcium chloride. Temperature was measured by a thermometer in the catalyst near the point of entry of the gases, and was maintained at 200—250° during reaction. Liquids were condensed from the products in a receiver at room temperature and in a trap at −78°.

The catalyst was heated in hydrogen to 300—350° before each day's working. It remained active and produced similar condensates throughout 3 months' use.

For the distillation analysis of the lower-boiling products, a 120-cm. Podbielniak column was used. Reflux cooling was provided by alcohol at about −50° for distillation below some 20°, and by a stream of air for liquids boiling above this region.

RESULTS AND DISCUSSION.

(i) *Effect of Temperature on the Reaction over a Catalyst of Steady Activity.*—Table I summarises data for the times (in mins.) necessary for the total pressure to fall by 100 mm. (t_{100}) and 200 mm. (t_{200}) for hydrogen : acetylene ratios of 1 : 1, 1 : 2, and 2 : 1. The plots of $\log_{10} t_{100}$ and $\log_{10} t_{200}$ against $1000/T$ (T = absolute temperature) are good straight lines, each of slope 2·85 with respect to the $1000/T$ axis.

The shapes of the total pressure–time curves (plotted to a scale expressed in fractions of t_{200}) showed little variation within each of two groups of experiments: (*a*) runs with 1 : 1 and 1 : 2 hydrogen : acetylene mixtures; (*b*) those with 2 : 1 hydrogen : acetylene ratio. The slight variations in curve shape showed no clear relationship to temperature and were probably due in part to temporary minor variations in catalyst activity. There were no signs that the dependence of the rate on the partial pressures differed anywhere between 0° and 91° from that found at 79° (Part I), and hence t_{100} and t_{200} were approximately the same, at a given temperature, for 1 : 1 and 1 : 2 hydrogen : acetylene mixtures, and reaction in the presence of twice the hydrogen pressure was about twice as fast.

For the calculation of activation energies, use was made of the initial rate of fall in total pressure, $(-\mathrm{d}p/\mathrm{d}t)_0$. Fig. 1 shows the plot of $\log_{10}(-\mathrm{d}p/\mathrm{d}t)_0$ against $1000/T$. Straight lines were obtained, of slope

TABLE I.

No. of expt. in series.		Temp.	$\log_{10}t_{100}$.	$\log_{10}t_{200}$.	No. of expt. in series.		Temp.	$\log_{10}t_{100}$.	$\log_{10}t_{200}$.
35	Initial pressures: 197—202 mm. H_2; 197—202 mm. C_2H_2.	0—3°	3·508	3·907	36	Initial pressures: 199—201 mm. H_2; 400—403 mm. C_2H_2.	0—3°	3·502	3·866
13		16—18	3·146	3·477	32		17—19	2·950	3·341
16		31	2·407	2·833	31		40	2·179	2·584
14		42	2·203	2·596	30		72	1·354	1·774
15		52	1·908	2·320	29		91	0·968	1·346
17		62	1·591	2·013	34	Initial pressures: 399—403 mm. H_2; 199—202 mm. C_2H_2.	0—3	3·322	3·607
23		71	1·335	1·782	33		17—19	2·486	2·817
18		81	1·130	1·556	25		30	2·114	2·436
22		94	0·845	1·262	26		50	1·547	—
19		103	0·720	1·114	27		50	1·500	1·860
20		114	0·464	0·829	24		71	0·929	1·248
21		126	0·30	0·65	28		91	0·52	0·79

$-2·64$ with respect to the $1000/T$ axis, and once again the effects of gas pressures on the rates were as noted in the preceding paragraph.

The gaseous products were analysed after falls in pressure of 200 mm. The results are plotted against temperature in Figs. 2 and 3. Production of ethylene and, more markedly, of ethane increased as the temper-

FIG. 2.

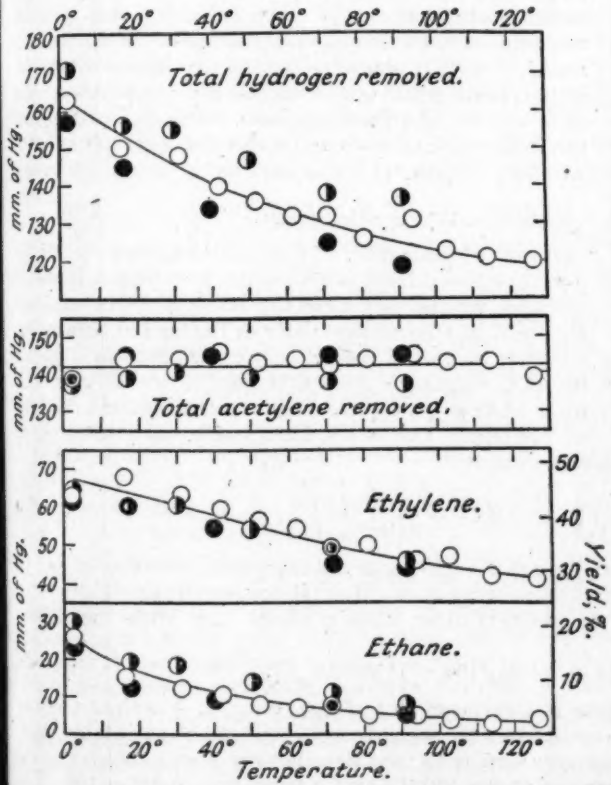
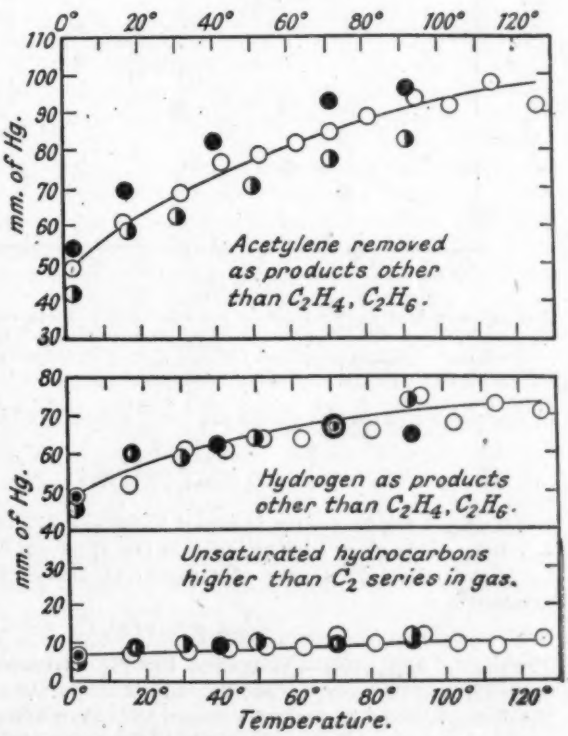


FIG. 3.


Acetylene removed as products other than C_2H_4, C_2H_6.
Hydrogen as products other than C_2H_4, C_2H_6.
Unsaturated hydrocarbons higher than C_2 series in gas.
mm. of Hg.
Temperature.

Figs. 2 and 3: *Initial pressures for each type of point are the same as in* Fig. 1.

ature was lowered. Correction for a possible slight error due to unobserved condensation of less volatile products during withdrawal of gas would increase this effect of temperature on the yields. The total amount of hydrogen removed increased with decreasing temperature, but the total amount of acetylene removed was within 5 mm. of 142 mm. in all the experiments. The approximate yield scale shown in Fig. 2 is calculated on the basis of a removal of 142 mm. of acetylene in each run. The amounts of acetylene and hydrogen removed as products other than C_2 hydrocarbons were about equal at 0°, but the amount of acetylene increased more markedly than that of hydrogen as the temperature was raised.

The effects of gas ratio on the amounts of gases formed and removed at a given temperature were small. The possible errors are larger in quantities which are the differences of pressures (especially the amounts of gases removed as products other than C_2 hydrocarbons, which are obtained by difference from three partial pressures in the product and the initial pressures), but with the present standardised experimental technique variations should be detected more readily than the estimated maximum absolute errors may suggest. Higher

hydrogen : acetylene ratios appeared slightly to favour ethane production, hydrogen removal, and acetylene recovery. Removal of acetylene as products other than C_2 hydrocarbons was probably less at the higher hydrogen : acetylene ratios. The effects of the partial pressures on the yields of C_2 hydrocarbons (expressed in terms of the acetylene not recovered) appear on the whole similar at temperatures between 0° and 91° to those found at 83° (Part I) over a very similar catalyst. This is seen from Fig. 4, in which $\log_{10} y$ (y = total yield of C_2 hydrocarbons) is plotted against $1000/T$; reasonable straight lines are obtained for each type of mixture, y increasing, at a given temperature, with hydrogen : acetylene ratio. In a few runs over different specimens of nickel–pumice, values of y slightly higher than in the present series of results were found for temperatures above about 80° (Part I, Table I), but in some such cases the high speed of reaction may have caused increased errors.

The effect of temperature on the yields is qualitatively in harmony with earlier work (*e.g.*, Sabatier and Senderens, *loc. cit.*) and with claims that yields of C_2 hydrocarbons can be increased by closer control of temperature by such means as suspension of the catalyst in a liquid (B.P. 294,787; Fischer and Peters, *Brennstoff-Chem.*, 1931, **12**, 286) or addition of gases such as nitrogen, carbon dioxide, or methane to the reaction mixture (U.S.P. 1,308,777; D.R.-P. 350,429; see also D.R.-P. 262,541; Dupont and Lombard, *loc. cit.*).

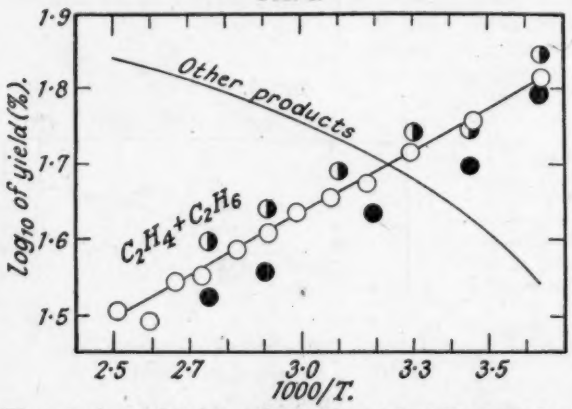
It is clear that the reaction yielding ethylene and ethane has a lower apparent heat of activation than the process by which acetylene and hydrogen are removed as other products. To obtain figures for activation energies it is necessary to make assumptions about the initial reaction, based on the temperature dependence of the products after a pressure fall of 200 mm. Since the total acetylene removed was independent of temperature (Fig. 2) it seems reasonable to assume that the initial rate of removal of acetylene is a constant fraction of $(-\mathrm{d}p/\mathrm{d}t)_0$ at all temperatures. The plot of $\log_{10}$ of the initial rate of removal of acetylene against $1000/T$ will then be parallel to the lines in Fig. 1, and therefore

$$\mathrm{d}\{\log_{10}(-\mathrm{d}[C_2H_2]/\mathrm{d}t)_0\}/\mathrm{d}(1000/T) = -2{\cdot}64$$

between 0° and 126°. It is also assumed that the initial rate of ethane production is zero (which is made probable by the fact that the ethylene yield exceeds the yield of ethane, especially at higher temperatures) and that the initial rate of ethylene formation is given by $(\mathrm{d}[C_2H_4]/\mathrm{d}t)_0 = (-\mathrm{d}[C_2H_2]/\mathrm{d}t)_0 y$, where y is the total yield of C_2 hydrocarbons after a fall in pressure of 200 mm. This is not improbable, since the effects of gas pressures on the yields are very small. It then follows that

$$\frac{\mathrm{d}}{\mathrm{d}(1000/T)}\left\{\log_{10}\left(\frac{\mathrm{d}[C_2H_4]}{\mathrm{d}t}\right)_0\right\} = -2{\cdot}64 + \frac{\mathrm{d}\log_{10} y}{\mathrm{d}(1000/T)}$$

FIG. 4.



The experimental points refer to the total yield of ethylene and ethane, those for the yield of other products being omitted. Initial pressures for each type of point are the same as in Fig. 1.

From Fig. 4 the last term is found to be +0·275 in the range 0—126°, and the expression becomes equal to −2·365. This gives 10·9 kg.-cals. as the apparent activation energy of reaction (I) between 0° and 126°.

If r is the initial rate of removal of acetylene as products other than ethylene, then with the above assumptions

$$\mathrm{d}\log_{10} r/\mathrm{d}(1000/T) = -2{\cdot}64 + \mathrm{d}\log_{10}(100 - y)/\mathrm{d}(1000/T).$$

The plot of $\log_{10}(100 - y)$ against $1000/T$ corresponding to the linear plot of $\log_{10} y$ in Fig. 4 is shown as the curved line in the same figure; the individual points are omitted for the sake of clarity, but can be calculated from the data plotted; they cluster round the curve in a way very similar to that in which the points shown cluster round the straight line. The slope of the curve with respect to the $1000/T$ axis is given by $-0{\cdot}275y/(100 - y)$ at any point, which gives a value of −0·12 at 126°, becoming more negative as the temperature falls, reaching −0·51 at 0°. Substitution in the last equation gives $\mathrm{d}\log_{10} r/\mathrm{d}(1000/T)$ values between −2·78 and −3·15. This gives 12·7 kg.-cals. as the apparent activation energy of reaction (II) at 126°; at 0° the value given is 14·5 kg.-cals. Intermediate figures are obtained at temperatures between these limits, *e.g.*, 13·4 kg.-cals. at 36°, where $y = 50$.

The reaction kinetics (Part I) indicate that these activation energies should each be corrected by addition of the heat of desorption of hydrogen.

Extrapolation of the straight line in Fig. 4 would predict values of y increasing as the temperature falls and reaching 100% at about −40°, the slope of the curved line meanwhile becoming more negative and tending to infinity as y approaches 100%; *i.e.*, the heat of activation of reaction (II) should increase, approaching infinity in the region of −40°. This does not seem probable, and the phenomena below 0° require further investigation. Extrapolation of the straight line in Fig. 4 to higher temperatures would predict values of y falling to about 26% in the region of 180°, whereas, in a flow-experiment (one of a series to be reported in detail later) over a

very similar catalyst (Ni-1, Part I) at 178°±5°, y was found to be about 40% for a 1 : 1 gas mixture at a total pressure of 1 atm. (ethylene yield 35%, ethane yield 5%; 94% of the acetylene removed in a contact time of 6 seconds). Extrapolations of the above types do not therefore seem justified.

Flow experiments of the type referred to above indicated that the total rate of reaction was probably still increasing with temperature in the region of 150—200°.

(ii) *Hydrocarbon Products Higher than the* C_2 *Series.*—The condensate in the receiver at room temperature (condensate 1) was yellow or brown, and was formed at about the same rate as the colourless condensate in the trap at −78° (condensate 2). Uncondensed gas emerged at about a quarter of the total rate of gas entry. No extensive deposition of carbon occurred.

About two-thirds of condensate 1 distilled from 60° to 310° with steadily rising b. p.; roughly one-sixth distilled from 100°/30 mm. to 250°/6 mm., leaving a gummy residue of about one-sixth. The colour deepened with rising b. p.

On distillation of condensate 2 through the Podbielniak column, about half passed over from −10° to 0° without distinct plateaux, and the remainder principally at 60—70°. A sample of gas given off by condensate 2 at room temperature contained about 75% of unsaturated hydrocarbons higher than the C_2-series, and some 25% of saturated hydrocarbon with an average of 4·8 carbon atoms per molecule. A test for butadiene in condensate 2 by the Diels–Alder reaction with maleic anhydride gave only a rubber-like product.

About 100 c.c. of condensate 2 were hydrogenated at 60—70° and 60—80 atm. over Raney nickel for 24 hours, absorption of gas then being complete. A 33% loss accompanied this process; this must be mainly a loss of the most volatile components. The residue was subjected to Podbielniak distillation, and the distillate boiling above 30° divided into cuts of roughly 1 c.c., the refractive indices (and, in certain cases, densities) of which were measured. A fully hydrogenated cut from the higher-boiling condensate (b. p. 176—200°) was added as a driving liquid. Boiling-point plateaux were observed at −4° to 0° (7 c.c.), 30—35° (4 c.c.; $n_D^{20°}$ of last two c.c. 1·3563 and 1·3591), 60—63° (35 c.c.; $n_D^{20°}$ rising from 1·3753 to 1·378 after 3 c.c., then steadily to 1·3830; $d_{15°}^{15°}$ 0·670—0·682), 86—96° (3 c.c.; $n_D^{20°}$ 1·3911—1·3960, $d_{15°}^{15°}$ 0·695—0·697), and 110—120° (4 c.c., $n_D^{20°}$ 1·4031—1·4050, $d_{15°}^{15°}$ 0·720—0·722). The rises in temperature between the plateaux were fairly steep, especially at the lower temperatures. There were no maxima or minima in the curve of $n_D^{20°}$ against volume distilled.

Some 160 c.c. of condensate 1 were hydrogenated over Raney nickel at 80—100 atm. and 200—220° for 72 hours, after which absorption of gas was extremely slow. About 7 l. of hydrogen were taken up. The product, which had a faint green fluorescence, was fractionated into: (*a*) a colourless fraction (through 10″ Dufton column), b. p. 60—200°, 55 c.c.; (*b*) a fraction beginning colourless and becoming pale yellow with rising b. p., b. p. 200—320°, 52 c.c.; (*c*) a brown viscous residue. Fraction (*a*) was distilled through the Podbielniak column, and cuts of about 1 c.c. examined. After a slight plateau (2 c.c.) in the b. p. curve at 62—67° ($n_D^{20°}$ 1·3758—1·3805) and an incline at about 90—112° (3 c.c.; $n_D^{20°}$ 1·3950—1·4033), a fairly well-defined plateau was found at 112—124° (12 c.c.; $n_D^{20°}$ 1·4030—1·4095, $d_{15°}^{15°}$ 0·728—0·735). The b. p. and $n_D^{20°}$ then rose fairly continuously, reaching 176° and 1·4259, respectively, after 40 c.c. had distilled. No maxima or minima were observed in the refractive index, plotted against volume distilled. The residue of fraction (*a*) (b. p. 176—200°) was not examined. Fraction (*b*) was distilled through a 10-cm. glass-packed column heated electrically to 20° below the distilling temperature, cuts of 1—2 c.c. being taken. The first 48 c.c. distilled with almost continuous rise in b. p. from 200° to 320° and in $n_D^{20°}$ from 1·4352 to 1·4701.

The physical properties of the cuts are those of paraffins, though pure fractions were not obtained, presumably on account of the complexity of the mixtures. There is no indication in the refractive indices of any appreciable formation of benzene or *cyclo*hexane, though the refractive indices and densities of the lower fractions are slightly higher than those of paraffins of the same b. p., which suggests that traces of substances of higher refractive index and density are present. The b. p. plateaux and approximately the expected physical properties show that butanes, pentanes, hexanes, heptanes, and octanes are probably present. The refractive indices provide conclusive evidence of the presence of pentanes. The liquid boiling higher than the octane plateau is doubtless a complex mixture of hydrocarbons from about C_9 upwards. The yellow colour and fluorescence of the higher-boiling products after intense hydrogenation show that some aromatic derivatives are probably formed.

Samples of the lower-boiling hydrogenated products were submitted to Dr. H. W. Thompson, to whom the author is indebted for an examination of their infra-red absorption spectra. For the samples of b. p. 33—90° the spectra leave little doubt as to the principal constituents, despite the fact that the b. p. values recorded are sometimes rather lower than expected from the composition. The paraffins found, with the approximate compositions of each cut, are listed in Table II, in which the volume figures refer to the stages at which the cuts were taken from the Podbielniak distillation of condensate 2 after hydrogenation.

Although time did not permit a further fractionation into purer samples, it is clear that the bulk of the hydrogenated C_6 fraction is made up of *n*-hexane and 3-methylpentane. The b. p. plateau in the region of −4° to 0° is fairly good evidence of the presence of *n*-butane (b. p. −0·5°; *iso*butane, b. p. −11·7°), and when it is remembered that much of the lowest-boiling products were lost in completing their hydrogenation, it is seen that the yield of *n*-butane may well have been large. The carbon skeletons of *n*-butane, *n*-hexane, and 3-methylpentane are the simplest which can be formed from C–C units without separating the carbon atoms. It thus appears probable that the products other than C_2 hydrocarbons are all formed principally by a linking

TABLE II.

Position of cut in distillation (c.c.).	B. p.	Composition.
9—10	33—35°	*ca.* 75% *n*-Pentane, *ca.* 25% 2-methylbutane.
11—12	51—58	*n*-Hexane, 2- and 3-methylpentane; probably no 2 : 3- or 2 : 2-dimethylbutane.
12—14	58—61	*n*-Hexane, 2- and 3-methylpentane, roughly 33% each.
18—20	62	*n*-Hexane, 3-methylpentane; <10% 2-methylpentane.
30—32	62—63	About equal amounts of *n*-hexane and 3-methylpentane.
40—42	63	
45—46	63	*n*-Hexane; not above 20% of 3-methylpentane.
46—47	63—66	*n*-Hexane; some 3-methylpentane, less than in preceding cut.
48—49	86—88	At least 50% 3-methylhexane. Almost certainly *n*-heptane. Possibly traces of 2 : 2-dimethylpentane. Probably no 2 : 4- and 3 : 3-dimethylpentanes.
49—50	88—89	As preceding cut. Slightly less 3-methylhexane.

together of C–C units in this way. Those which cannot be so formed (*e.g.*, 2-methylpentane, pentanes, heptanes) must be produced by isomerisation or cracking at some stage; this stage may be the final one, or it may be followed by addition of one or more C–C units before the final structure is attained. It is unlikely that any extensive isomerisation accompanied the high-pressure hydrogenation of the liquid products.

The results for the C_6 fractions resemble those of Antsus and Petrov (*loc. cit.*, 1942) for nickel–zinc chloride; in the present experiments, however, no 2 : 3-dimethylbutane structures were detected, and the predominance of *n*-hexane structures was not so marked, the yield of 3-methylpentane being almost as large as that of *n*-hexane, with a distinctly smaller amount of 2-methylpentane. Much larger yields of C_4 compounds were found in the present work than under rather similar conditions by Petrov and Antsus (*loc. cit.*, 1934).

The amounts of unsaturated gases higher than ethylene found in products from experiments at lower temperatures (see, *e.g.*, Fig. 3) are about $\frac{1}{7}$ to $\frac{1}{10}$ of the amounts of acetylene removed by reaction (II), the products of which must therefore be largely of relatively low molecular weight at these temperatures also. Reduced polymers of acetylene, chiefly of low molecular weight, are apparently formed over a number of metals, such as iron, cobalt, platinum, and, under certain conditions, copper (*e.g.*, Sabatier and Senderens, *Compt. rend.*, 1900, **130**, 1628, 1559; **131**, 40). Work to be published later has confirmed this, and shown that the reduced polymers formed over palladium also have a relatively low mean molecular weight. The formation of " benzine " from acetylene and hydrogen over mixed metal catalysts is well known (*e.g.*, *inter alia*, Peters and Neumann, *Ges. Abh. Kenntn. Kohle*, 1934, **11**, 423). The main products appear to be aliphatic, and in the few cases where any close study has been made (*e.g.*, Neumann, *ibid.*, p. **434**, for iron–nickel catalysts) there is a general similarity to the products over nickel, *e.g.*, large formation of hexenes.

On the basis of the distillation data, the products of reaction (II) over nickel–pumice in the present experiments can be estimated to contain the following approximate percentages by weight: C_4 hydrocarbons 25%, C_5 hydrocarbons 1—2%, C_6 hydrocarbons 25%, C_7 hydrocarbons 1—2%, C_8 hydrocarbons 5%, with some 7% in the range C_9 to (very roughly) C_{14} and about 17% in each of the ranges C_{14} to (very roughly) C_{30} and C_{30} to C_x, where x is unknown but large. If molecular percentages are used the predominance of lower members is even more marked. In more accurate flow experiments under roughly the same conditions the yield of products other than C_2 hydrocarbons was 60—70%; if this applies also to the large-scale experiments, the yields of the cuts listed above will be obtained in terms of the acetylene not recovered by multiplying the appropriate percentages by 0·6—0·7.

(iii) *General Discussion.*—It should be emphasised that, though hydrogenation of acetylene to ethane is quantitative with a large excess of hydrogen on platinum (Conn, Kistiakowsky, and Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 1868), this is exceptional; the normal reaction on all the catalysts so far investigated is accompanied by some formation of hydrocarbons higher than the C_2 series (see, *e.g.*, Sabatier and Senderens, *locc. cit.*; Pichler, *Ges. Abh. Kenntn. Kohle*, 1934, **11**, 395; Ackermann, *Brennstoff-Chem.*, 1937, **18**, 357; Yoshikawa, *Bull. Chem. Soc. Japan*, 1932, **7**, 201; Cremer, Knorr, and Plieninger, *Z. Elektrochem.*, 1941, **47**, 737; etc.). In contrast, the hydrogenation of ethylene is always virtually a quantitative reaction on metal catalysts.

Reference was made in Part I to the ready formation of hydrocarbons higher than the C_2 series from acetylene and hydrogen over nickel under conditions of temperature and acetylene pressure under which the same catalysts caused very little reaction in acetylene alone. This type of phenomenon is probably general among metal catalysts, except those containing appreciable amounts of copper, which has a marked polymerising action on acetylene (see, *e.g.*, Egloff, " The Reactions of Pure Hydrocarbons," 1937). The primary action of hydrogenation catalysts on acetylene alone appears usually to be a decomposition rather than a polymerisation (see, *e.g.*, Egloff, *op. cit.*), yet in the presence of hydrogen hydrocarbons higher than the C_2 series are formed. In the case of nickel there is evidence that a linking together of C–C units without rupture is the primary reaction; this probably applies also to other metals, though more experimental evidence is needed here.

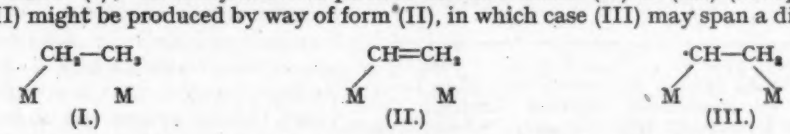
Over nickel the formation of hydrocarbons higher than the C_2 series is a first-order reaction with respect to hydrogen. Determination of orders of reaction is more difficult with other catalysts, but it appears probable that the phenomena on palladium are not unlike those on nickel, and that the resemblance may extend to other catalysts also. Results with catalysts other than nickel will be reported in detail later.

Local overheating of the catalyst by the primary hydrogenation reaction is a totally inadequate explanation of the phenomena outlined above, despite the fact that acetylene is more readily polymerised than ethylene (cf. Damköhler, *Z. physikal. Chem.*, 1943, *A*, **193**, 16). Except in the case of copper, moreover, the overheated

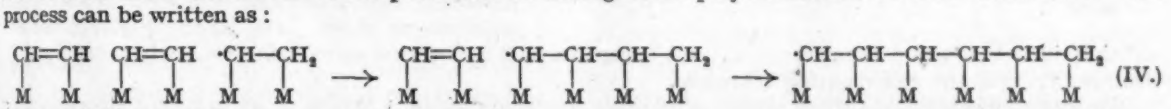
metal would be expected to decompose acetylene rather than polymerise it. Acetylene is more strongly adsorbed than ethylene on nickel (see Part I), platinum (Farkas and Farkas, *J. Amer. Chem. Soc.*, 1939, **61**, 3396), palladium (Cremer, Knorr, and Plieninger, *loc. cit.*), iron (work to be published later) and probably other metals, but this is not a satisfactory explanation of the difference in behaviour of these hydrocarbons on hydrogenation, since it has been maintained that ethylene can completely cover a nickel surface (Twigg and Rideal, *Trans. Faraday Soc.*, 1940, **36**, 533; *Proc. Roy. Soc.*, 1939, *A*, **171**, 55). Greater separation of the points of unsaturation for steric reasons may account for the fact that alkylacetylenes do not appear to polymerise as readily as acetylene itself when hydrogenated (see, *e.g.*, Campbell and Campbell, *Chem. Reviews*, 1942, **31**, 77).

The greater unsaturation of acetylene as compared with ethylene is a more probable cause of the difference in behaviour of these hydrocarbons on hydrogenation. Herington (*Trans. Faraday Soc.*, 1941, **37**, 361) has pointed out how this difference in degree of unsaturation is especially emphasised if the concept of associative two-point adsorption is correct, since acetylene so adsorbed is still unsaturated, whereas ethylene so adsorbed is not. He cites as evidence for this mode of adsorption the polymerisation of acetylene over cobalt in the presence of hydrogen, compared with the quantitative hydrogenation of ethylene to ethane over that metal. The importance of the presence of hydrogen needs stronger emphasis for the reasons given above.

The part played by hydrogen can be explained, without the supposition of such factors as overheating of the catalyst, by a development of the theory of associative adsorption. The formation of a " half-hydrogenated " state has been frequently postulated in the mechanisms of exchange reactions and double-bond migration in olefins according to the theory of associative adsorption (*e.g.*, Twigg and Rideal, *loc. cit.*, 1939; Rideal, *Proc. Camb. Phil. Soc.*, 1939, **35**, 130; *Chem. and Ind.*, 1943, **62**, 335; Twigg, *Proc. Roy. Soc.*, 1941, *A*, **178**, 106) and, by other authorities, also in the hydrogenation itself on metals (*e.g.*, Horiuti and Polanyi, *Trans. Faraday Soc.*, 1934, **30**, 1164; Greenhalgh and Polanyi, *ibid.*, 1939, **35**, 520). For ethylene this state is a bound ethyl radical (I); for acetylene it is possible to write either (II) or (III) (M represents a catalyst atom). Form (III) might be produced by way of form (II), in which case (III) may span a different M–M space



from that originally adsorbing the acetylene. State (III) differs from states (I) and (II) in having a carbon atom with one unpaired electron, and is in this sense a free radical, though still adsorbed on the catalyst. It is then possible to formulate polymerisation by a chain reaction in associatively adsorbed acetylene, resembling the radical-chain mechanisms often postulated in homogeneous polymerisations of olefin derivatives. The process can be written as :



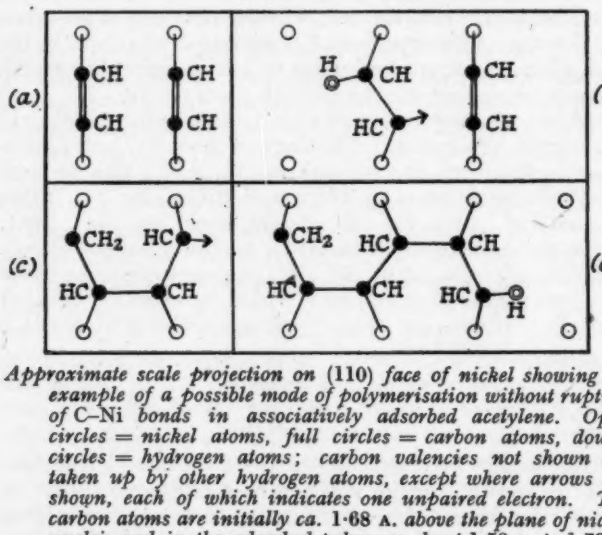
(IV.)

and so on. In the absence of hydrogen, state (III) cannot be formed, which explains the lack of appreciable polymerisation under those conditions on catalysts other than copper; on that metal, other factors make a mechanism of initiation by hydrogen less necessary. Polymerisation as above could not occur in associatively adsorbed ethylene; since, however, it is not impossible that unsaturated molecules in van der Waals layers above the chemisorbed layer could become involved in the reaction chain, the essential difference between the hydrogenation of ethylene and of acetylene according to these concepts rests at least as much in the possibility of a different type of half-hydrogenated state in acetylene, as in the fact that associatively adsorbed acetylene is still unsaturated, though that fact probably contributes considerably to the causes of the observed phenomena. With adsorptions described as physical (*e.g.*, Hansford and Emmett, *J. Amer. Chem. Soc.*, 1938, **60**, 1185) or dissociative (*e.g.*, Farkas, *Trans. Faraday Soc.*, 1939, **35**, 906), both of which leave acetylene and ethylene unsaturated, the different behaviour of these gases on hydrogenation would have to be explained in terms of such factors as denser packing or more ready polymerisation in acetylene. The polymerisation of ethylene on hydrogenation catalysts can occur, *e.g.*, on nickel at 240—360° (Pscheshetzki and Gladischev, *J. Physical Chem. U.S.S.R.*, 1941, **15**, 333), and has even been reported on very active nickel at room temperature (Morikawa, Trenner, and Taylor, *J. Amer. Chem. Soc.*, 1937, **59**, 1103), but is in general much slower than polymerisation in the acetylene–hydrogen system under comparable conditions. There is no evidence that ethylene polymerisation on metals is promoted by hydrogen.

A study of scale models has been made to determine in what circumstances the type of polymerisation suggested for acetylene in the presence of hydrogen is reasonably possible on steric grounds. Bond lengths used were : C–C 1·54 A., C=C 1·33 A., C–Ni 2·0 A. In nickel the (100) face cannot accommodate forms of the type of (IV), though it may adsorb acetylene. The (111) face might accommodate, with some strain, a C_4 or C_6 polymer, but is probably unsuitable for the associative adsorption of acetylene (Herington, *loc. cit.*). The (110) face, however, would permit a polymer to form from acetylene adsorbed associatively on 3·50 A. spaces without rupture of C–Ni bonds, the increase in strain being insufficient to make the process unlikely. Fig. 5 illustrates the type of mechanism. It is assumed that state (III) is formed from acetylene without rupture of C–Ni bonds, strain being relieved by rotation about the C–C bond (Fig. 5*b*; in this discussion the stereochemistry of a carbon atom with 7 valency electrons is assumed to be the same as that of normal carbon, the

unpaired electron replacing one valency). Such rotation may bring the carbon deficient in electrons towards an adjacent acetylene molecule in the manner shown (Fig. 5*b*), and steric conditions are now probably suitable for a change to a *n*-C_4 radical (Fig. 5*c*). At this stage the strain is shown distributed among the valency angles (C$\widehat{\text{C}}$–C = *ca.* 115°, C–C$\widehat{\text{–Ni}}$ = *ca.* 103° across 2·48 A. spaces, *ca.* 115° across 3·50 A. spaces); the necessary distortions from the normal angles are thus probably not large enough to prevent the changes suggested. Interaction of the C_4 radical with another acetylene molecule in the same way is seen to be possible, but in the *n*-C_6 skeleton produced (Fig. 5*d*) the central portion must be under somewhat greater strain than previously (C$\widehat{\text{C}}$–C increases to about 127°; distortions in C–C$\widehat{\text{–Ni}}$ are a little less than before). Since, however, by analogy with gaseous polymerisation of olefins, we expect a considerable release of bond energy (of the order of 17 kg.-cals./mol.) for every acetylene unit added to the radical, such increase in strain may well not make the reaction thermodynamically impossible; if so, the polymer chain could be extended indefinitely as long as acetylene molecules became suitably positioned. In Fig. 5*d* the chain is shown terminated at the C_6 stage by addition of a hydrogen atom, and some redistribution of strain in the terminal C–C units is again assumed.

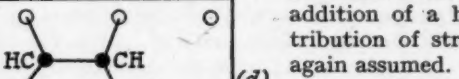
FIG. 5.



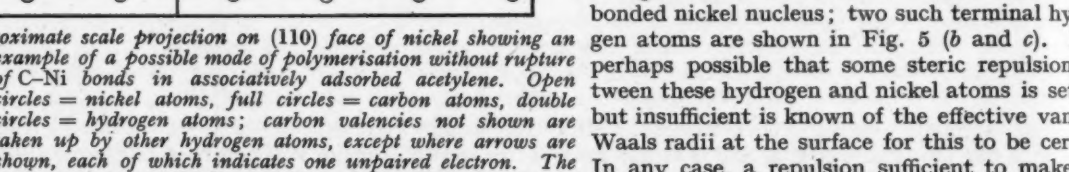
Approximate scale projection on (110) *face of nickel showing an example of a possible mode of polymerisation without rupture of* C–Ni *bonds in associatively adsorbed acetylene. Open circles = nickel atoms, full circles = carbon atoms, double circles = hydrogen atoms; carbon valencies not shown are taken up by other hydrogen atoms, except where arrows are shown, each of which indicates one unpaired electron. The carbon atoms are initially ca.* 1·68 A. *above the plane of nickel nuclei, and in the adsorbed polymers about* 1·58 A. *to* 1·73 A. *above it.*

A possible objection to the above is that one hydrogen nucleus of the terminal $>CH_2$ groups is brought within about 2·6 A. of the nearest non-bonded nickel nucleus; two such terminal hydrogen atoms are shown in Fig. 5 (*b* and *c*). It is perhaps possible that some steric repulsion between these hydrogen and nickel atoms is set up, but insufficient is known of the effective van der Waals radii at the surface for this to be certain. In any case, a repulsion sufficient to make the above processes impossible is unlikely. We note, however, that acetylene adsorbed on a space adjacent to state (III) (as in Fig. 5*b*) would certainly impede rotation about the C–C bond except in such a direction as to bring the carbon deficient in electrons towards the neighbouring acetylene.

Formation of branched carbon skeletons presents greater difficulty. Attack of an unpaired electron on a C–Ni bond, *e.g.*,



or on a C=C link in a desorbed part of a polymer appears in general improbable for steric reasons. A mechanism involving migration of a hydrogen atom, on a (110) face, is sterically more likely, and an example is shown below.



If states (III) and (II) could be formed as shown, the radical (V) may be produced with migration of hydrogen, and might then add acetylene molecules in the manner shown in Fig. 5, yielding 3-methyl derivatives, *e.g.*, the 3-methylpentane structure. Variations on this process can be formulated.

This yields branched structures without rupture of the original C_2 skeletons. Other branched structures, *e.g.*, of the 2-methylpentane type, can only be formed by way of such a rupture, and this may account for the relatively large amounts of 3-methyl- as compared with 2-methyl-pentane, found in the present experiments. The " cross-polymerisation " mechanism proposed by Antsus and Petrov (*loc. cit.*, 1942), besides leaving out of account the promotion of reaction by hydrogen, does not distinguish so sharply between the methods of production of 2- and 3-methylpentane structures.

It is desirable, however, that the products of reaction (II) at temperatures below 200° should be examined more closely before it is concluded with certainty that there is this distinction between the two methods.

Polymerisation by the suggested mechanisms may be facilitated by desorption (with hydrogenation or otherwise) of parts of the polymer, though by no means all such processes at first sight possible are likely on

steric grounds. Many of the products are certainly hydrogenated beyond the stage attained by the polymerisation of adsorbed acetylene induced by state (III). Since migration of double bonds is expected to accompany the reaction, the positions of these in the products are of uncertain value as evidence in deciding the mechanism. It is clear that, with the suggested processes, unsaturation can appear at numerous parts of the polymer.

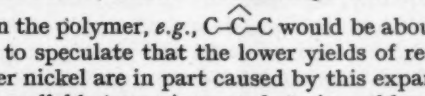
While strain may tend to oppose production of long polymer molecules in the above manner, other factors can also favour short chain length. In particular, if a (110) face is covered with acetylene, at random except for the condition that 3·50 A. spaces be spanned, an arrangement of n adjacent molecules abreast (as in Fig. 5*a*) becomes more improbable as n increases. The proportion of unoccupied metal atoms in an immobile orientated film of molecules in two-point contact of this type can be shown to be 13·53% by a calculation used in another connexion by Flory (*J. Amer. Chem. Soc.*, 1939, **61**, 1518). The number of groups of n adjacent molecules (excluding any contained in groups of more than n) will then be the fraction $(0{\cdot}5677)^2(0{\cdot}4323)^{n-1}$ of the number of molecules chemisorbed. For $n = 1, 2, 3, 4$, and 5 the fractions are 32·2%, 13·9%, 6·0%, 2·6%, and 1·1%, respectively. Mobility of the film to reduce the number of unoccupied atoms raises the contribution of larger groups at the expense of the smaller ones, but the decline in number of groups with increase in n is still rapid. Experiments with a model of the (110) face (400 atoms), in a manner similar to that used by Roberts (*Proc. Camb. Phil. Soc.*, 1938, **34**, 399), gave results satisfactorily close to those calculated. If the adsorption of acetylene and mechanism of polymerisation are as postulated above, the improbability of large groups of adjacent acetylene molecules may well play a part in causing the predominance of low molecular-weight reduced polymers from acetylene and hydrogen on various metals. Ethylene can presumably be formed on the (110) face also, but probably without intermediate formation of a half-hydrogenated state (see below). Arrangements from which branched polymers may be formed without rupture of C–C units (as discussed above) appear about as probable in the orientated chemisorbed film as arrangements suitable for production of isomeric normal structures; this is not out of keeping with the formation of comparable amounts of *n*-hexane and 3-methylpentane.

In the above treatment it has been assumed that the probability of adsorption of acetylene on a site is independent of the occupation or otherwise of adjacent sites. This is probably unjustified; for example, as was indicated in Part I, molecules adsorbed as in Fig. 5*a* are likely to be subject to mutual steric repulsion on account of the bulk of the carbon atoms; the non-bonded carbon–carbon distance of 2·48 A. may be compared with the interlayer distance in graphite, 3·4 A. Tilting of the molecules may thus occur, and such an effect would further reduce the probability of two or more molecules being adsorbed abreast on adjacent spaces. This probability would also fall if the adsorption film became unsaturated with respect to acetylene, as might happen for example at temperatures above those at which reaction orders could be determined in the present experiments.

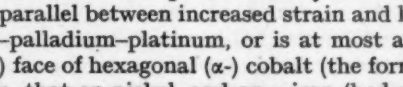
The strain set up in polymerisation as in Fig. 5 is increased by extension of the lattice distances, notably by reason of the increase in C–$\widehat{\text{C}}$–C necessitated by the expansion of the shorter spacings. If acetylene is again assumed to span the longer distances, the increase in strain on polymerisation on (110) faces of β(cubic)-cobalt and copper is little larger than in the case of nickel. On the larger face-centred cubic lattices of palladium and platinum more strain is expected in the polymer, *e.g.*, C–$\widehat{\text{C}}$–C would be about 140° in the central part of a structure like Fig. 5*d*. It is tempting to speculate that the lower yields of reduced polymers over palladium and platinum compared with those over nickel are in part caused by this expansion of the lattice, but so simple an explanation is unlikely, since the parallel between increased strain and lower yield of polymers does not extend outside the vertical group nickel–palladium–platinum, or is at most applicable only to face-centred lattices. Thus polymerisation on the (01$\bar{1}$0) face of hexagonal (α-) cobalt (the form stable below 400°) sets up a structure similar to, but more strained than, that on nickel, and on α-iron (body-centred cubic) a polymerisation of the type suggested is quite unlikely on steric grounds, unless, *e.g.*, many C–Fe bonds are broken and re-formed; yet considerable amounts of reduced polymers are formed over both iron and cobalt. Such comparisons show that deductions made from purely steric considerations of a relatively simple mechanism are largely speculative, as can only be expected since many factors, particularly some specific to the metal, must be ignored in the steric model. In addition, the surface lattice may be modified by reaction. It is also possible, as previously mentioned, to formulate mechanisms in which states such as (III) initiate polymerisation in acetylene in a van der Waals layer, where the influence of the lattice is expected to be greatly diminished.

Until many more results are available, the suggested initiation of reaction (II) by the half-hydrogenated state (III) is at least useful in accounting for some general aspects of acetylene hydrogenation-polymerisation.

The reaction chains discussed could be terminated in various ways. These include (*a*) mutual combination of radicals, (*b*) mutual disproportionation of radicals, (*c*) interaction of the unpaired electron with hydrogen, *e.g.*, in a van der Waals layer (compare Rideal, *locc. cit.*),



and (*d*) ejection of a hydrogen atom, *e.g.*,



Methods (*a*) and (*c*) appear, in general, the most likely on steric grounds. The carbon deficient in electrons might also complete its octet by the removal of a C–metal bond, either as mentioned in discussing branched structures, or within the same radical, as in changes analogous to that from state (III) to state (II). Except in special cases, such as the last-named, these changes are improbable for steric reasons; moreover, since an electrically neutral hydrocarbon with an even number of electrons cannot be desorbed at such a stage, the polymerisation is not truly terminated. Besides the cases (*a*)—(*d*) above, some other possible termination mechanisms are indicated below.

Since the mean chain length is short, propagation and termination must proceed at comparable rates. The simplest kinetic analysis is obtained by assuming that propagation and termination are both much faster than the initiation of chains, and that the chain length is independent of the hydrogen pressure. The observed data could then be accounted for by a rate-determining formation of state (III) from strongly adsorbed acetylene and weakly adsorbed hydrogen, *e.g.*, van der Waals hydrogen in the manner proposed by Rideal. If this initiation step has the energy of activation observed for reaction (II) (12·7—14·5 kg.-cals.), this step does not appear to be involved in ethylene production, since the activation energy in that case is lower. This suggests that ethylene is formed by simultaneous addition, to strongly adsorbed acetylene, of two hydrogen atoms from the same weakly adsorbed hydrogen molecule, which is in harmony with mechanisms at present favoured for hydrogenation in general on metals (*e.g.*, Twigg and Rideal, *Proc. Roy. Soc.*, **1939**, *A*, **171**, 55; Rideal, *Chem. and Ind.*, **1943**, **62**, 335; Farkas and Farkas, *Trans. Faraday Soc.*, **1937**, **33**, 837; Farkas, *loc. cit.*). It is, however, difficult to reconcile the assumption made above, *viz.*, that the chain length is independent of the hydrogen pressure, with the termination mechanisms at first sight most acceptable, *i.e.*, mutual termination, or termination by hydrogen in a manner not unlike the initiation process. With such terminations the chain length is expected to decrease as the hydrogen pressure is raised, and the order of reaction (II) with respect to hydrogen would be less than that of the initial step, *i.e.*, less than unity, since it is unlikely that initiation will be of order higher than the first with respect to hydrogen. If future experiment shows that the chain length is in fact independent of the hydrogen pressure, other modes of termination are indicated, such as spontaneous or monomer termination, though these are unexpected with radical chains. Alternatively, termination might be by some other species, of concentration independent of the hydrogen pressure; such a species might be atomic or molecular hydrogen adsorbed on certain special sites, *e.g.*, uncovered catalyst atoms. If termination involves addition of a hydrogen atom, some factor (*e.g.*, a steric one) presumably prevents appreciable ethylene formation by termination at state (III), otherwise the difference in heats of activation of reactions (I) and (II) is difficult to explain. This difference, other factors being equal, is expected to lead to a greater contribution of ethylene formation to the reaction than is found, a mean chain length of 10 or less being allowed for polymerisation (the observed mean length at 200—250° is about 4). Other factors besides the activation energy, therefore, probably differ slightly for the two types of reaction, favouring reaction (II) somewhat.

A greater complexity than indicated above is quite possible. For instance, although propagation as in Fig. 5 may be relatively fast (as in some analogous vinyl polymerisations of homogeneous type) provided acetylene molecules are suitably placed, it is not impossible that propagation and termination can be slow enough to influence the kinetics profoundly, especially if additional steps occur involving migration of radicals on the catalyst, *e.g.*, as in the suggested mechanism of formation of branched structures; a complex series of successive reactions then takes place. An attempt at general kinetic analysis is almost certainly premature, the difficulties being magnified by the heterogeneous nature of the reaction and the fact that the chains are predominantly short, with several possible modes of termination. Explanation of the observed order with respect to hydrogen again presents some difficulty. Other complicating factors have already been indicated; to these should be added the possibility of deposition of polymers on the catalyst, especially in so far as it may affect the observed heats of activation. Propagation of chains in the gas phase and decomposition of acetylene might also occur, but there is no evidence that the extent of either process is sufficient to demand modification of the main arguments of the discussion.

The slight difference in orders of reactions (I) and (II) (Part I) is presumably to be explained in terms of a greater proportion of hydrogen in the adsorption layers at higher hydrogen : acetylene ratios, in such a way as to favour ethylene production somewhat, at the expense of polymerisation, but an attempt to interpret this and other smaller details of the results more precisely is speculative in view of the more general uncertainties.

Closer elucidation must await knowledge of the structures of the products at *ca.* 100° or less (especially contributions of branched structures), and study of the effects of temperature and gas pressures on the chain length and distribution of structures in the products of reaction (II).

The author has pleasure in thanking Mr. D. Ll. Hammick for much help and advice, and the Department of Scientific and Industrial Research for a grant.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, September 29th*, 1944.]

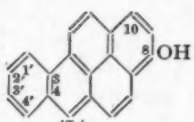
37. *The Direct Hydroxylation of* 1′ : 2′ : 3′ : 4′-*Tetrahydro*-3 : 4-*benzpyrene.*

By George A. R. Kon and Edna M. F. Roe.

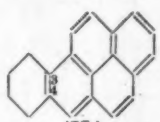
Lead tetra-acetate attacks 1′ : 2′ : 3′ : 4′-tetrahydro-3 : 4-benzpyrene almost exclusively in the saturated ring, giving the 1′-acetoxy-compound (III, R = COMe) and a hydrocarbon formulated as 3′ : 4′-dihydro-3 : 4-benzpyrene (IV). Acetoxy-derivatives substituted in the pyrene ring system are only formed in small amount.

When the carcinogenic hydrocarbon 3 : 4-benzpyrene is injected into rats, a portion of it is excreted in the form of a hydroxylated derivative BPX (Chalmers and Crowfoot, *Biochem. J.*, 1941, **35**, 1270, and previous publications). Evidence that BPX is 8-hydroxy-3 : 4-benzpyrene (I) has been adduced (Berenblum and Schoenthal, *Cancer Res.*, 1943, **3**, 145; Berenblum, Crowfoot, Holiday, and Schoenthal, *ibid.*, p. 151), and it appeared of great interest to attempt to synthesise this compound in view of its bearing on the problem of the mechanism by which carcinogenic compounds are detoxified in the animal body.

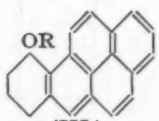
A possible route to the desired compound was indicated by the observation of Vollmann, Becker, Corell, and Streeck (*Annalen*, 1937, **531**, 1) that pyrene is first substituted in position 3, but the next substituent enters position 8 or 10; *e.g.*, a mixture of the 3 : 8- and the 3 : 10-quinones is obtained on oxidation. It would therefore be expected that 1′ : 2′ : 3′ : 4′-tetrahydro-3 : 4-benzpyrene (II), which is, in effect, a 3-substituted pyrene, would be further substituted in position 8 or 10. For the introduction of the desired substituent, direct hydroxylation with lead tetra-acetate, which has been frequently used in polycyclic compounds (Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1938, **60**, 1893, 2542) appeared to offer an easy route to the tetrahydro-derivatives of the required compounds, which could then be dehydrogenated.



(I.)



(II.)



(III.)

4′-Keto-1′ : 2′ : 3′ : 4′-tetrahydrobenzpyrene (Cook and Hewett, J., 1933, 398; Fieser and Fieser, *J. Amer. Chem. Soc.*, 1935, **57**, 782) affords the hydrocarbon (II) in moderate yield when reduced by the Clemmensen method (*idem*, *ibid.*; Bachmann, Carmack, and Safir, *ibid.*, 1941, **63**, 1682) and for this reason Fieser and Fieser recommend catalytic reduction at high temperature and pressure in presence of copper chromite; however, an excellent yield of the hydrocarbon has now been obtained by the modified Kishner–Wolff technique (Kon and Soper, J., 1940, 1335). The hydrocarbon has the properties already described by Fieser and Fieser and Bachmann *et al.*, and the higher m. p. quoted by Winterstein, Vetter, and Schön (*Ber.*, 1935, **68**, 1079) could not be confirmed; the compound has been further characterised by means of its trinitrobenzene *compound*.

Hydroxylation of the hydrocarbon with lead tetra-acetate was tried under a variety of conditions. The separation of the products was tedious, but could be achieved by repeated chromatographic adsorption. The course of the separation could be conveniently observed in ultra-violet light; one of the principal products was a *hydrocarbon*, $C_{20}H_{14}$, with a violet fluorescence, and a more adsorbable fraction with a greenish-blue fluorescence consisted of acetoxy-compounds.

Of the latter, only one could be obtained in reasonable amount for investigation. Hydrolysis by the action of methylmagnesium iodide was not satisfactory, but alkaline hydrolysis readily gave a non-phenolic *hydroxy*-compound (III, R = H), which was oxidised by the Oppenauer method to the corresponding *ketone*, m. p. 174—175° depressed by admixture of the 4′-ketone of the same m. p. It is clear that the acetoxy-group must have entered the saturated ring of the hydrocarbon (II), as it does in methylcholanthrene (Fieser and Hershberg, *loc. cit.*, p. 2542); its position on C$^{1'}$ was demonstrated by treating the above ketone with methylmagnesium iodide. The product was dehydrated and heated with sulphur, whereby 1′-methyl-3 : 4-benzpyrene was formed; it had m. p. 190—191° and gave a crimson trinitrobenzene compound, m. p. 208—209°, in agreement with the findings of Bachmann and Carmack (*J. Amer. Chem. Soc.*, 1941, **63**, 2494).

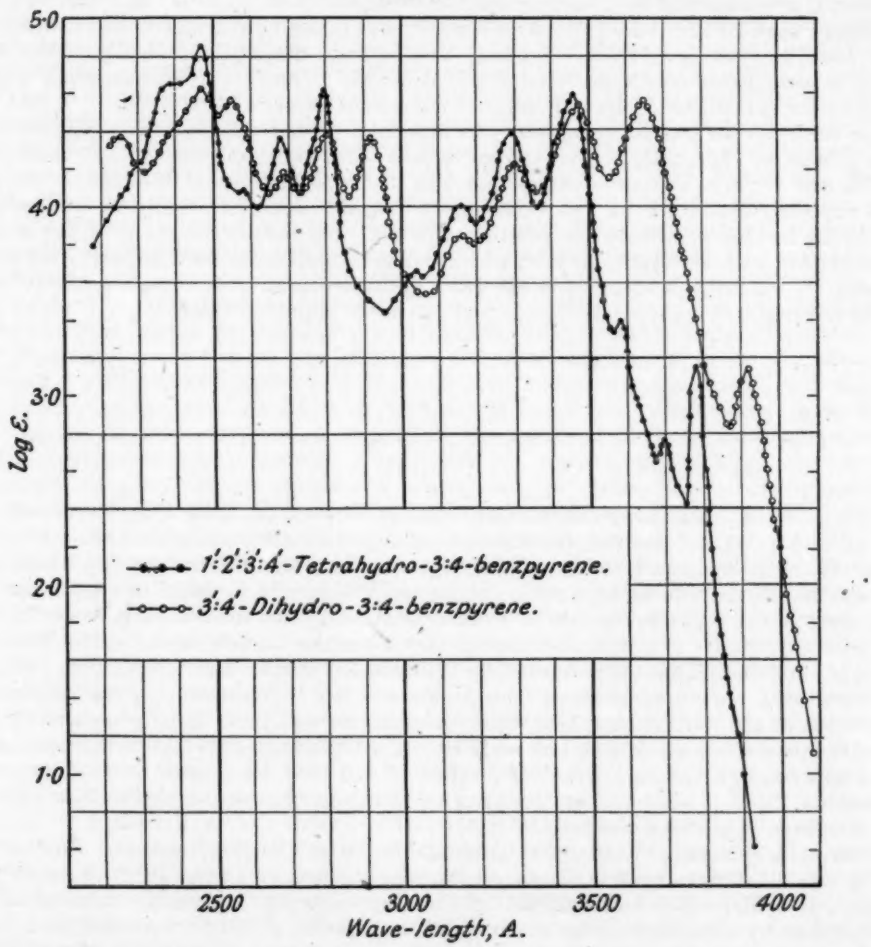
The acetoxy-compound (III, R = Ac) is accompanied by at least two isomerides, m. p.'s 161—162° and 155°, but their formation is uncertain and the amounts formed are always small. At least one of them is a phenolic derivative, because when the crude acetoxylation product containing them was hydrolysed and methylated a methyl ether, m. p. 110—112°, was obtained; this is probably the desired 8(or 10)-*methoxy-tetrahydro*-3 : 4-*benzpyrene*.

The *hydrocarbon* also formed in this reaction can be separated from the small amount of unchanged hydrocarbon (II) by repeated chromatographic adsorption; it melts at 128° and mixtures of it with (II) (m. p. 113°) melt at intermediate temperatures, and the same applies to their trinitrobenzene compounds (m. p. 202—203° and 198—199°, respectively), but there can be little doubt that they are not identical and the new hydrocarbon is a dihydro-3 : 4-benzpyrene isomeric with the compound described as 1′ : 2′-dihydro-3 : 4-benzpyrene by Bachmann and Carmack (*ibid.*, p. 1685). Since acetoxylation of tetrahydrobenzpyrene takes place mainly on C$^{1'}$, it seems reasonable to suppose that the new double bond will be introduced between C$^{1'}$ and C$^{2'}$ with the formation of 3′ : 4′-dihydro-3 : 4-benzpyrene (IV). In an endeavour to confirm the structure of this compound,

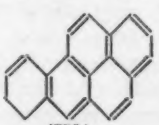
its absorption spectrum and those of tetrahydrobenzpyrene and of Bachmann and Carmack's dihydrobenzpyrene have been measured.

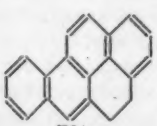
The tetrahydro-compound shows a typical pyrene spectrum (Fig. 1) and requires no comment. Our 3′ : 4′-dihydro-compound also has a spectrum of the pyrene type (Fig. 1), but the intensities of the principal maxima are reduced and the peaks displaced towards the visible region, an effect compatible with the greater weight of the molecule and the additional double bond in conjugation with those of pyrene. The spectrum of Bachmann and Carmack's compound (Fig. 2) differs appreciably from that of its isomeride and is related to the chrysene rather than the pyrene type of spectrum. In particular, the similarity to the spectrum of 4 : 5-di-

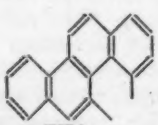
FIG. 1.



methylchrysene (VI) (Jones, *ibid.*, p. 313), which is reproduced for comparison, is striking. In the absence of other evidence, this suggests that Bachmann and Carmack's hydrocarbon is more correctly formu-


(IV.)


(V.)


(VI.)

lated as 6 : 7-dihydro-3 : 4-benzpyrene (V), which can be regarded as a 4 : 5-disubstituted chrysene and is formed by a rearrangement of the double bonds of the expected 1′ : 2′-dihydro-compound.

Other possible synthetic approaches to the compound BPX have been explored without success, such as the reaction of 3-methoxypyrene with acetyl chloride or succinic anhydride, which gave inseparable mixtures; attempts to introduce a hydroxyl group into 3-acetylpyrene by way of the nitro-compound or by sulphonation were also fruitless.

EXPERIMENTAL.

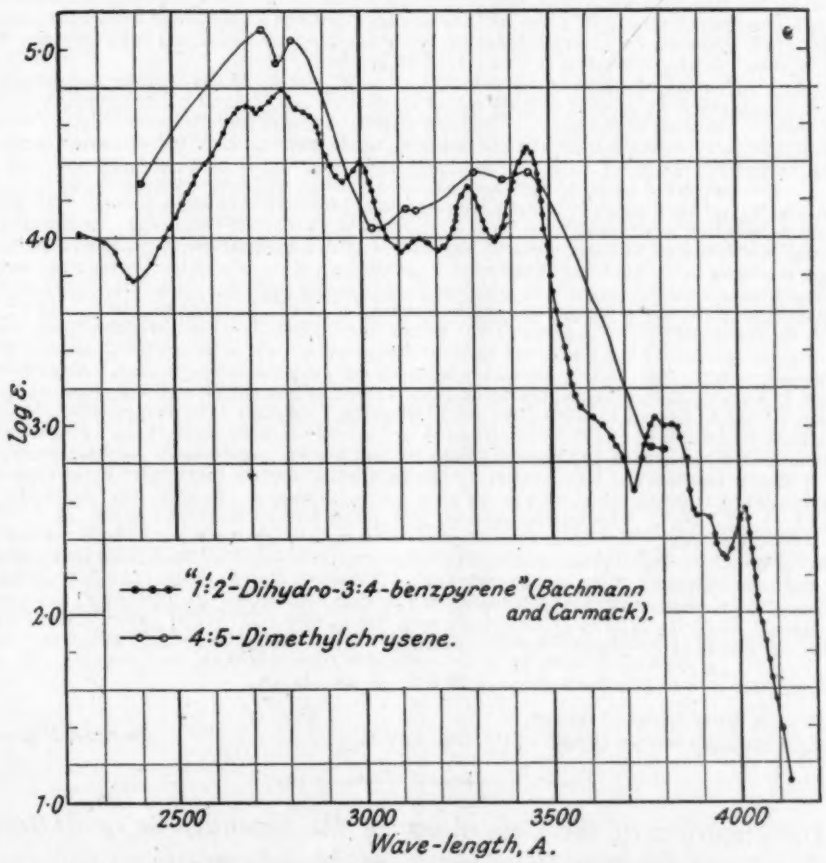
1′ : 2′ : 3′ : 4′-*Tetrahydro*-3 : 4-*benzpyrene*.—Four sealed tubes, each containing 2 g. of 4′-keto-1′ : 2′ : 3′ : 4′-tetrahydro-3 : 4-benzpyrene, 4·5 c.c. of 99% hydrazine hydrate, and 32 c.c. of a 5% solution of sodium in alcohol, were heated

at 200° for 16 hours. The hydrocarbon was extracted with light petroleum (b. p. 60—80°) in which the unchanged ketone is virtually insoluble; the last traces of ketone can be removed by percolating the washed and dried solution through a column of alumina (Spence, type H). The yield of hydrocarbon obtained by evaporation of the solution is 85%, and 7% of unchanged ketone can be recovered. The reduction of the ketone was also successfully carried out on a 20-g. scale in a stainless-steel autoclave of 500 c.c. capacity.* The trinitrobenzene *compound* crystallises from benzene–alcohol in orange-red needles, m. p. 198—199° (Found : C, 66·5; H, 4·3. $C_{26}H_{19}O_6N_3$ requires C, 66·5; H, 4·1%).

7 G. of the hydrocarbon in 32 c.c. of carbon tetrachloride were kept ice-cold and mechanically stirred while 4 g. of chlorosulphonic acid were slowly run in, the stirring being continued for a further 6 hours. After distillation of the solvent, the dark green, gummy material was treated with 30 c.c. of water, and the solution saturated with salt. The dark solid was collected, dried, and added to 30 g. of fused sodium hydroxide (bath at 270° rising to 300° in 10 minutes). The cooled melt was dissolved in water, and the solution repeatedly filtered from a brown amorphous powder. The filtrate was saturated with carbon dioxide, causing a flocculent precipitate, but no definite product could be isolated from it.

Action of Lead Tetra-acetate.—This reagent was prepared as described by Dimroth and Schweitzer (*Ber.*, 1923, **56**, 1375), recrystallised from acetic acid, and dried in a desiccator. The oxidations were carried out under varying conditions and in different solvents, *viz.*, petroleum, benzene, or mixtures of these. The following is a typical experiment : 10·2 g. of the hydrocarbon in 540 c.c. of " AnalaR " benzene were added to 16·2 g. of lead tetra-acetate suspended in

FIG. 2.



900 c.c. of " AnalaR " acetic acid, the resulting clear brown solution being kept overnight. It was then diluted with much water, the benzene layer separated off, repeatedly shaken with water, finally with sodium carbonate solution, filtered from a sludgy precipitate of lead salts, dried over sodium sulphate, and diluted with its own volume of petroleum (b. p. 60—80°). The solution was percolated through a short, wide column of activated alumina (Spence, type H), which was washed with the same solvent. The colourless solution gave on evaporation a greenish oil which soon solidified. It was dissolved in 1·5 l. of petroleum and percolated through 100 g. of alumina, the column being then washed with 1·5 l. of the same solvent; the petroleum solution gave 3 g. of solid (A) on evaporation. The column was eluted with 3 l. of 1 : 1 petroleum–benzene, which removed 4·5 g. of solid (B). Very little more material was recovered by elution of the column with pure benzene.

(A) was still a mixture melting below 100° and could be resolved by further chromatography in petroleum into unchanged tetrahydrobenzpyrene, which comes through in the first runnings, leaving another hydrocarbon adsorbed on the column. This was eluted with benzene–petroleum and could be purified by way of the picrate, forming brownish-purple needles from benzene–alcohol, m. p. 174—175°, or the trinitrobenzene *compound*, crimson-red needles from benzene–alcohol, m. p. 202—203° (Found : C, 66·4; H, 3·8. $C_{26}H_{17}O_6N_3$ requires C, 66·8; H, 3·7%), from which the *hydrocarbon* (IV) could be regenerated by percolating a benzene solution through alumina. It crystallised from alcohol

* The authors are greatly indebted to Prof. I. M. Heilbron, D.S.O., F.R.S., for permission to carry out this reduction at the Imperial College of Science and Technology.

in pale buff plates, m. p. 128° (Found: C, 94·3; H, 5·7. $C_{20}H_{14}$ requires C, 94·4; H, 5·6%), which tend to darken when exposed to light.

The fraction (B) was repeatedly crystallised from alcohol or from acetone–methanol, forming fine, iridescent, flattened needles, m. p. 174—175°, consisting of 1′-*acetoxy*-1′ : 2′ : 3′ : 4′-*tetrahydro*-3 : 4-*benzpyrene* (III, R = Ac) (Found: C, 84·2; H, 5·7. $C_{22}H_{18}O_2$ requires C, 84·0; H, 5·8%). The best yield (70% of material crystallised once) of this compound was obtained when the reaction mixture was kept at room temperature for 20 mins., then warmed for 45 mins. on the steam-bath, the benzene being then distilled off under reduced pressure. The products were isolated by addition of water and extraction with ether; the solid recovered from the extract was finally chromatographed in benzene–petroleum and crystallised from acetone–methanol.

Isomeric Acetoxy-compounds.—By a tedious fractional crystallisation from alcohol, ethyl acetate, or petroleum, these were isolated in small amounts in acetoxylation experiments performed at room temperature. One of these compounds forms colourless iridescent plates which look pale green in ordinary light owing to their intense fluorescence, which is blue in ultra-violet light, and melt at 161—163° (Found: C, 84·2; H, 6·0. $C_{22}H_{18}O_2$ requires C, 84·0; H, 5·8%). Another compound isolated in very small amount has a green fluorescence in ultra-violet light and melts at about 155° (Found: C, 84·3; H, 5·8%); it is more strongly adsorbed on alumina than the isomeride of m. p. 161—163°.

x-*Methoxy*-1′ : 2′ : 3′ : 4′-*tetrahydro*-3 : 4-*benzpyrene*.—The crude mixture of acetoxy-compounds (0·4 g.) obtained by eluting the column of alumina with benzene after removal of the hydrocarbons (cf. p. 145) was boiled with 2 g. of potassium hydroxide, 2 c.c. of water, and 40 c.c. of methyl alcohol for an hour, cooled, treated with an excess of methyl sulphate, and the process repeated several times. The excess of reagent was finally hydrolysed with more alkali, and the product isolated by dilution with water was recrystallised from alcohol. The solid obtained after repeated crystallisation was the acetoxy-compound, m. p. 155°; the mother-liquors deposited a compound with a similar green fluorescence, but melting at 110—112° after repeated crystallisation from ethyl acetate–alcohol, evidently the *methoxy*-compound (Found: C, 88·4; H, 6·5. $C_{21}H_{16}O$ requires C, 88·1; H, 6·3%).

1′-*Hydroxy*-1′ : 2′ : 3′ : 4′-*tetrahydro*-3 : 4-*benzpyrene* (III, R = H).—2 G. of the acetoxy-compound, m. p. 174—175°, were boiled with 7 g. of potassium hydroxide and 150 c.c. of alcohol, 20 c.c. of water being gradually added to the solution in the course of 45 mins. The bulk of the alcohol was then distilled off, and more water added. The *hydroxy*-compound (1·5 g.) was collected and recrystallised from alcohol, forming thick prisms, m. p. 180—181° (Found: C, 88·1; H, 6·1. $C_{20}H_{16}O$ requires C, 88·2; H, 5·9%).

1′-*Keto*-1′ : 2′ : 3′ : 4′-*tetrahydro*-3 : 4-*benzpyrene*.—2·65 G. of crude hydroxy-compound, 25 c.c. of *cyclo*hexanone, 135 c.c. of benzene, and 9 g. of aluminium *tert.*-butoxide were boiled for 16 hours under reflux. The product was isolated by washing the benzene solution with dilute acid, drying, diluting with its own volume of petroleum (b. p. 60—80°), and percolating it through a column of alumina. Some difficulty was experienced owing to the presence of *cyclo*hexanone and its condensation products in the eluate, but these were distilled off in a high vacuum after evaporation of the solvent. The *ketone* crystallised from benzene–petroleum and from ethyl acetate–alcohol in sulphur-yellow plates, m. p. 174—175°, depressed by admixture of the 4′-ketone (Found: C, 88·8; H, 5·3. $C_{20}H_{14}O$ requires C, 88·9; H, 5·2%).

1′-*Methyl*-3 : 4-*benzpyrene*.—0·6 G. of the ketone was added to a Grignard reagent prepared from 0·2 g. of magnesium, 1·5 c.c. of methyl iodide, and 15 c.c. of ether, the mixture being boiled under reflux for 5 hours. It was decomposed with ice and dilute hydrochloric acid, the ethereal solution washed, dried, and evaporated. The residue was heated for 6 hours to 130—150° at a pressure of 0·5 mm., the formation of a crystalline sublimate being observed. 0·1 G. of sulphur was now added, and the whole heated to 230—240° for 30 minutes, evolution of hydrogen sulphide then having ceased. On distillation in a high vacuum a hard solid was obtained, apparently in very good yield. It was dissolved in benzene and treated with an excess of picric acid, the resulting dark reddish-brown picrate being once recrystallised from benzene; m. p. 182—183°. The *hydrocarbon* was regenerated by percolating a benzene solution of the picrate through a column of alumina, and crystallised from benzene–alcohol in pale yellow plates, m. p. 190—191° (Found: C, 94·6; H, 5·4. $C_{21}H_{14}$ requires C, 94·7; H, 5·3%). The trinitrobenzene compound formed crimson needles, m. p. 208—209°.

1′ : 2′-*Dihydro*-3 : 4-*benzpyrene* (V?).—This was prepared as described by Bachmann and Carmack (*loc. cit.*, p. 1685); the best product was obtained by decomposition of the pyridinium salt isolated by them, and was purified by sublimation in a high vacuum and crystallisation from benzene–alcohol. It formed plates, m. p. 148—149°, unchanged by further crystallisation. The trinitrobenzene *compound* formed dark orange needles, m. p. 199—200°, after crystallisation from benzene–alcohol (Found: C, 67·3; H, 3·9. $C_{26}H_{17}O_6N_3$ requires C, 66·8; H, 3·7%). Mixtures of this compound with the trinitrobenzene compounds of tetrahydro- and the isomeric dihydro-benzpyrene melt at intermediate temperatures.

The authors' thanks are due to Mr. F. Goulden, A.R.I.C., for assistance.

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38. *An Investigation of the Occurrence of the Co-ordinate or Dative Link by Electric Dipole-moment Measurements.*

By G. M. PHILLIPS, J. S. HUNTER, and L. E. SUTTON.

'In the early formulations of the higher oxides and oxy-acids of elements in Groups V, VI, and VII, the oxygen atoms attached only to a central atom were supposed to be held by double bonds. According to Lewis, however, they are held by co-ordinate or dative links; and this view received support from stereochemical investigations.

Subsequent measurements of the bond lengths threw serious doubt on the later formulations for such compounds of elements not in the first short period, and suggested that the earlier ones were more correct. Electric dipole-moment data gave some support to this conclusion.

In this paper, more dipole-moment measurements are reported. The changes of moment which occur when phosphines and sulphides form links to oxygen or sulphur are compared with those when they form *complexes* with boron trifluoride or trichloride, in which the boron must accept a co-ordinate link, and these in turn with the changes when amines or ethers form links to the same atoms or groups.

The results, considered together with thermal data, show that the older formulations are much nearer the truth than the newer ones. The remarkable shortening of the links to less than the values expected for double bonds is shown to be an example of a rather general phenomenon, *viz.*, that abnormally strong bonds tend to be abnormally short.

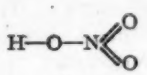
The corresponding bond in a phosphine imine is examined, with a less definite result—it may be derived more nearly equally from the two structures.

The remarkable compound dimethylsulphonium-9-fluorenylidide is found to be highly polar, showing that the attachment of the two parts of the molecule is by a co-ordinate link. It is probable that the substance exists only because of stabilisation by resonance in the ring system.

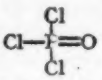
The structure of ozone is discussed. The low polarity and low stability are shown to be related.

The stable existence of the higher oxy-acids of the halogens can be considered as due to the formation of multiple links. Fluorine cannot form such links, however, nor is it likely to be able to form strong co-ordinate links: so the apparent non-existence of its higher oxy-acids is thus explicable.

In the early " nucleus " formulæ of the higher oxides and oxy-acids of the elements in Groups V, VI, and VII of the Periodic System, two assumptions were made. One was that the oxygen is always bivalent, forming either two single bonds or one double one; the other that the central or nucleus element can have a valency numerically equal to its group number. For example, in such compounds, nitrogen and phosphorus were supposed to be quinquevalent, sulphur sexavalent, and chlorine septavalent, as in (I)—(IV). Werner (" Neuere



(I.)



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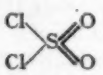

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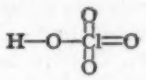
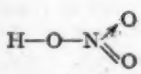


(IV.)

Anschauungen auf dem Gebiete der anorganischen Chemie," Braunschweig, 1905) objected to these formulæ on the grounds that they implied a distinction, which to him seemed artificial, between the oxy-acids and the halogeno-acids, *e.g.*, chloroplatinic acid; and also because not all of the double bonds postulated actually add on water. He remarked on the frequency with which elements in their most highly oxidised compounds are found associated with *four* oxygen atoms.

When, later, Lewis placed covalency on a physical basis by introducing the concept of electron sharing, he showed that it was possible to formulate many compounds, including the higher oxides and oxy-acids, with an octet of electrons round each atom (*J. Amer. Chem. Soc.*, 1916, **38**, 762). In place of some of the double bonds in the old formulations, he postulated single covalencies for which the central atom provides both shared electrons. This type of link was termed by Sidgwick (" The Electronic Theory of Valency," Oxford, 1927) the co-ordinate link; * and (I)—(IV) were replaced by (V)—(VIII).

This type of structure gained wide acceptance because it showed that such compounds could be formally unified with many others on the general principle that an atom strives in forming valencies to achieve an inert-gas structure, and so has a covalency limit of four. Application of Bohr's theory of atomic structure, and later of wave-mechanics, to valency problems strongly supported this principle as applied to elements in the first short period (see Pauling, " The Nature of the Chemical Bond," Cornell, 1940, p. 31); and though both theory and the actual existence of such compounds as phosphorus pentafluoride and sulphur hexafluoride showed that the limit of covalency is higher in the later periods, parachor measurements and observations on stereochemical properties appeared to support the octet formulæ for the oxy-compounds (see Sidgwick, *op. cit.*). The large electric moments, 4·1 and 5·1 D. respectively, for diphenylsulphoxide and diphenylsulphone (Bergmann, Engel, and Sandor, *Z. physikal. Chem.*, 1930, *B*, **10**, 397; de Vries and Rodebush, *J. Amer. Chem. Soc.*, 1931, **52**, 2888; Bergmann and Tschudnowsky, *Ber.*, 1932, **65**, 457) also appeared to do this. For a long time, therefore, these formulæ were accepted without serious question.



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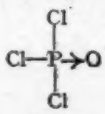

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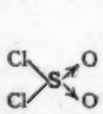

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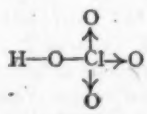


(VIII.)

This view was challenged in 1937 when Pauling and Brockway (*J. Amer. Chem. Soc.*, **59**, 13) drew attention to certain theoretical and practical difficulties. For dithionic and hypophosphoric acids the octet structures lead to large formal charges of like sign on adjacent atoms, which should cause marked instability. These authors suggested, therefore, that there is resonance between several possible structures in which double bonds hold one or more of the extra oxygen atoms. Their adjacent charge rule appears not to be of universal application (see Sutton, J., 1940, 551); but they also produced a more concrete objection, *viz.*, that the bond lengths in the common oxy-acid ions are much shorter than single bonds should be, being in fact as short as double bonds, or even shorter. Either, therefore, must co-ordinate links be much shorter than normal single bonds, or the bonds in question cannot be co-ordinate links.

Further investigations, on the one hand, revealed more examples of very short bonds to extra oxygen or sulphur atoms (which may conveniently be termed " oxy-bonds "), and on the other hand they gave information about the length of true co-ordinate links. Palmer and Elliott (*J. Amer. Chem. Soc.*, 1938, **60**, 1852)

* Objection has been made to this term (see, *e.g.*, Laubengayer and Finlay, *J. Amer. Chem. Soc.*, 1943, **65**, 884), but it has the merit of brevity; and provided that it be not applied to the solid state it does not cause confusion. Of the alternatives suggested, dative bond (Menzies, *Nature*, 1928, **121**, 457) seems the best.

measured the Al–X distance in the four-membered ring (IX) in the dimeric aluminium trihalides: these bonds may be regarded as hybrids between normal single bonds (Al–X) and co-ordinate links ($\overset{-}{Al}\leftarrow\overset{+}{X}$). For the chloride, bromide, and iodide they are 2·21±0·04, 2·33±0·04, and 2·58±0·04 A., in good agreement with the sums of the tetrahedral single-bond radius for aluminium (1·26 A., Pauling and Huggins, *Z. Krist.*, 1934, *A*, **87**, 205) and the normal radii for the halogens (Pauling, *op. cit.*, p. 164), *viz.*, 2·25, 2·40, and 2·59 A. Lister and Sutton (*Trans. Faraday Soc.*, 1939, **35**, 495) reported that the length of the N–O bond in trimethylamine oxide is 1·36±0·03 A. The length found for the N–O single link in *O*-methylhydroxylamine is *ca.* 1·43 A.; this length is that calculated by Schomaker and Stevenson (*J. Amer. Chem. Soc.*, 1941, **63**, 37), whereas the Pauling normal radii give 1·36 A., and 1·15 A. for a double bond, N=O; so the actual length is nearer to that expected for a single bond than for a double one,* and certainly is not *shorter* than the latter.

(IX.)

Moreover, Bauer, Finlay, and Laubengayer (*ibid.*, 1943, **65**, 889), from an electron-diffraction investigation of dimethyl ether–boron trifluoride, report that the length of the B–O bond therein is 1·52±0·06 A., *i.e.*, rather longer than the mean, 1·47 A., of the B–O bond lengths in the tetrahedrally co-ordinated boron phosphate and arsenate (Schultze, *Z. physikal. Chem.*, 1933, *B*, **24**, 215) wherein each boron, phosphorus, or arsenic atom is surrounded by four oxygen atoms, and each of the latter is shared between a phosphorus or arsenic and a boron atom. It is very close to the sum, 1·54 A., of the Pauling single-bond radii, or to the sum of Pauling's radius for oxygen and Bauer and Beach's radius for boron (0·85 A.), *i.e.*, 1·51 A., but somewhat larger than the value got by Bauer and Beach (*J. Amer. Chem. Soc.*, 1941, **63**, 1394) using their boron radius and Schomaker and Stevenson's correction (*loc. cit.*) for the supposed electronegativity difference, *viz.*, 1·45 A. True co-ordinate links appear, therefore, to be nearly of the length to be expected for a normal, single covalency between the same two elements.

In contrast, the bonds between elements of the second short period and the extra oxygen or sulphur atoms always prove to be as short as, or shorter than the normal double-bond length. This is shown by Table I (an elaboration of that in *Ann. Reports*, 1940, **37**, 75).

Two facts are especially striking. One is that the P–O′ bonds in $P_4O_6O_4'$ are extremely short and are thus differentiated from the P–O bonds which, although also shorter than theoretical single bonds, are much less abnormal. Secondly, from the lengthening of the C–S bond in dimethylsulphone ($l_{C\text{-}S}$ = 1·90±0·03 A. instead of 1·81; see Lister and Sutton, *loc. cit.*) the sulphur radius appears to be larger than it is in the normal bivalent state; yet the S–O bonds are very short. Bond-length data therefore suggest very strongly that the oxy-bonds are not co-ordinate links.

On more careful examination, electric dipole-moment data prove also to support this conclusion. The N–O bond in trimethylamine oxide is 1·36 A. long; so if an electron were completely transferred in the formation of the bond, and there were symmetrical sharing of the bonding electrons, the moment would be (electronic charge) × (bond length), *i.e.*, 6·53 D. The value derived by Linton (*J. Amer. Chem. Soc.*, 1940, **62**, 1945) and ourselves (see later) is 4·22—4·37 D., *i.e.*, 66—68% of theory. Moreover, the very large moments of certain co-ordination complexes show that they contain highly polar bonds, although it is true that in some of these the unco-ordinated molecules are themselves quite polar. Examples are: $(Et_2O)_2,BeCl_2$, 6·71 D.; $MeCN,BCl_3$, 7·74 D.; Et_2O,BCl_3, 6·04 D.; $EtNH_2,AlCl_3$, 6·94 D.; $Et_2O,AlCl_3$, 6·68 D.; $C_6H_5\cdot NO_2,AlCl_3$, 9·25 D.; $COPh_2,AlCl_3$, 8·32 D. (Nespital, *Z. physikal. Chem.*, 1932, *B*, **16**, 153); $(Et_2S)_2,PtCl_2$, 9·5 D.; $(Et_3P)_2,PtCl_2$, 10·7 D.; $(Et_3As)_2,PtCl_2$, 10·5 D.; $(Et_3Sb)_2,PtCl_2$, 9·2 D. (Jensen, *Z. anorg. Chem.*, 1935, **225**, 97; 1936, **229**, 225; 1937, **231**, 365).

If the S–O, P–O, and P–S bonds were co-ordinate links they should be even more polar than the N–O link, because they are actually longer: the moments for full transference would be 6·86, 7·44, and 9·31 D., respectively. The actual values ascribed are, however, 2·16—2·6 (Coop and Sutton, *Trans. Faraday Soc.*, 1939, **35**, 505), 3·5, and 2·5 D. (Smyth, *J. Amer. Chem. Soc.*, 1938, **60**, 183), respectively, *i.e.*, only 31·5—38%, 47%, and 27% of the theoretical values.

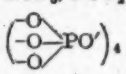
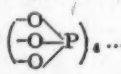
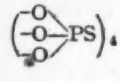
There is, therefore, a strong case against the theory that the S–O, P–O, and P–S bonds in these compounds are co-ordinate links. The data are, however, still relatively unsystematic. Moreover, it is not certain that

* On the very simple argument that, in the bond $\overset{+}{A}\text{–}\overset{-}{B}$, the formal positive charge on A probably decreases its radius as much as the negative charge on B increases its radius, Elliott (*J. Amer. Chem. Soc.*, 1937, **59**, 1380) predicted that the length of the co-ordinate link would be the same as that of a normal single bond between A and B. This is almost certainly an over simplification. A better, though still arbitrary, analysis would be to suppose that there are two effects: (i) the change of radii of the donor and acceptor atoms, brought about by the formal charges and the changes in valency state; (ii) the attraction between the formally charged atoms. The second factor will obviously tend to shorten the link; but it is by no means certain what the first will do. Some data indicate that the radius of a donor nitrogen atom is greater than the Pauling normal valency radius which is valid in amines (see Lister and Sutton, *loc. cit.*): Albrecht and Corey (*J. Amer. Chem. Soc.*, 1939, **61**, 1087) find, however, that in the glycine " zwitterion " the C–N distance in the group $CH_2\text{–}NH_3^+$ is only 1·39 A., *i.e.*, 0·08 A. less than predicted. Bauer, Finlay, and Laubengayer (*loc. cit.*) find no shortening of the C–O bonds in dimethyl ether–boron trifluoride, but rather a slight extension.

The effective radius of boron increases when it becomes an acceptor: $l_{B\text{-}F}$ in boron trifluoride is 1·30 ± 0·02 A., but in dimethyl ether–boron trifluoride it is 1·41 ± 0·02 A. It therefore seems possible that both the donor and the acceptor atoms undergo an increase of radius, but that this is more or less counterbalanced by the increased mutual attraction arising from their formal charges.

TABLE I.

Oxy-bond Lengths.

Compound.	$l_{obs.}$, A.	Method.	Ref.
Sulphur–oxygen bonds.			
$l_{calc.}$, A. (Pauling's radii) ‡ : single, 1·70*; double, 1·49; triple, 1·37.			
$SOMe_2$	1·46	E.D.†	(a)
SO_2Me_2	1·44 ± 0·03	—	(a′)
SO_2	1·43 ± 0·01	—	(b)
SO_3, SO_2Cl_2, SO_2F_2	1·43 ± 0·02	—	(c), (d)
$SOCl_2$	1·45 ± 0·02	—	(c)
$S_2O_3^{--}$, $S_2O_6^{--}$, SO_4^{--} (Li_2SO_4)	1·50	*X*-Ray cryst.	(e), (f), (g)
SO_4^{--} ($CaSO_4$, Na_2SO_4)	1·49	—	(h), (i)
SO_4^{--} (Ag_2SO_4)	1·48	—	(j)
SO_3^{--} (Na_2SO_3)	1·39	—	(k)
$S_2O_5^{--}$	1·46	—	(l)
$K{\cdot}SO_3{\cdot}NH_2$	1·44 ± 0·03	—	(m)
Phosphorus–oxygen bonds.			
$l_{calc.}$, A. : single, 1·76*; double, 1·57; triple, 1·43.			
POF_3, POF_2Cl, $POFCl_2$, $POCl_3$	1·55 ± 0·03	E.D.	(n)
	PO′ 1·39 ± 0·02 PO 1·62 ± 0·02	—	(o)
	PO 1·65 ± 0·02	—	(o)
$NH_4H_2PO_4$	1·51 ± 0·11	*X*-Ray cryst.	(p)
KH_2PO_4	1·56	—	(p′)
Ag_3PO_4	1·61 ± 0·03	—	(q)
Phosphates	1·56	—	(r)
$(BPO_4)_n$	1·55	—	(s)
Phosphorus–sulphur bonds.			
$l_{calc.}$, A. : single, 2·14*; double, 1·94; triple, 1·80.			
$PSCl_3$	1·94 ± 0·03	E.D.	(t)
PSF_3	1·85 ± 0·02	—	(u)
	1·85 ± 0·02 (PO = 1·61 ± 0·02)	—	(u)
Chlorine–oxygen bonds.			
$l_{calc.}$, A. : single, 1·65*; double, 1·44.			
ClO_3^- ($NaClO_3$, $KClO_3$)	1·48	*X*-Ray cryst.	(k)
ClO_4^- ($KClO_4$, NH_4ClO_4)	1·44, 1·49	—	(v)
ClO_4^- ($MClO_4$)	1·56	—	(w)

* The single-bond lengths calculated by the method of Schomaker and Stevenson (*loc. cit.*) are : S–O, 1·69; P O 1·71; P–S, 2·10; Cl–O, 1·68$_5$ A.

† "E.D." means by electron-diffraction investigation of the vapour. "*X*-Ray cryst." means by *X*-ray diffraction investigation of the crystal.

‡ Pauling, *op. cit.*, p. 164.

(a) Rundle and Stevenson, unpublished. (a′) Lister and Sutton, *loc. cit.* (b) Schomaker and Stevenson, *J. Amer. Chem. Soc.*, 1940, **62**, 1270. (c) Palmer, *ibid.*, 1938, **60**, 2360. (d) Stevenson and Russell, *ibid.*, 1940, **62**, 3264. (e) Mooney and Zachariasen, *Physical Rev.*, 1933, (ii), **44**, 327. (f) Zachariasen, *Z. Krist.*, 1934, **89**, 529. (g) Albright, *ibid.*, 1932, **84**, 150. (h) Wooster, *ibid.*, 1936, **94**, 375. (i) Zachariasen and Ziegler, *ibid.*, 1932, **81**, 92. (j) Zachariasen and Hermann, *ibid.*, 1932, **82**, 161. (k) Zachariasen, *J. Amer. Chem. Soc.*, 1931, **53**, 2123. (l) *Idem*, *Physical Rev.*, 1932, (ii), **40**, 923. (m) Brown and Cox, J., 1940, 1. (n) Brockway and Beach, *J. Amer. Chem. Soc.*, 1938, **60**, 1836. (o) Hampson and Stosick, *ibid.*, p. 1814. (p) Zachariasen and Mooney, *J. Chem. Physics*, 1934, **2**, 34. (p′) West, *Z. Krist.*, 1930, **74**, 306. (q) Helmholtz, *J. Chem. Physics*, 1936, **4**, 316. (r) Wyckoff, "Structure of Crystals," 2nd Edn., 1931, pp. 192, 193. (s) Schulze, *Z. physikal. Chem.*, 1933, *B*, **24**, 215. (t) Beach and Stevenson, *J. Chem. Physics*, 1938, **6**, 75. (u) Stosick, *J. Amer. Chem. Soc.*, 1939, **61**, 1130. (v) Gottfried and Schresterius, *Z. Krist.*, 1932, **84**, 65. (w) Zachariasen, *ibid.*, 1931, **80**, 137.

a direct comparison of the moments of bonds to oxygen formed by elements in the first and the second short period can settle the point at issue, since the greater polarisability of the latter elements may affect the moments. We really need to know more certainly what the moments of the latter bonds would be if they were co-ordinate links.

We therefore determined the changes of moment which occur when phosphines and sulphides form links to oxygen or to sulphur, and those when they form complexes with boron trifluoride or trichloride; and, as far as possible, those when amines and ethers form links to the same atoms or groups.

Since the covalency of boron is limited to 4, the only kind of definite link which it can form in the complexes is a co-ordinate one. It cannot form a multiple link. Thus, we know the changes which occur when an element of the first short period forms dative links to oxygen or to boron, and when the corresponding

element in the second short period forms one to boron: therefore we can predict roughly what should be the change if the latter formed a dative link to oxygen. We can then say with some certainty whether or not the actual change is as great as it should be for the formation of a bond of this kind.

This work has been only briefly mentioned before (Sutton, *Ann. Reports*, 1940, **37**, 75). Some results recently reported by Jensen (*Z. anorg. Chem.*, 1943, **250**, 268) overlap ours, and will be considered with them.

As related matters of interest, attempts were made to establish the nature of the P–N link in triphenylphosphinephenylimine, and of the S–C link in the remarkable compound dimethylsulphonium-9-fluorenylidide.

This task was begun by one of us (J. S. H.) in 1937—1938, and continued (by G. M. P.) in 1938—1939; but then it was interrupted, and so is itself not really complete. A parallel investigation of bond lengths, by electron-diffraction studies, was commenced in 1938—1939, but it had to be abandoned.

Experimental.

Preparation and Purification of Materials.—Benzene (B.D.H. "AnalaR") was purified by being frozen out three times, refluxed over phosphoric oxide in a stream of dry air, and finally distilled in the dry air stream. It was stored under dry air until used (Hampson, Farmer, and Sutton, *Proc. Roy. Soc.*, 1933, *A*, **143**, 147).

(Preparations by J. S. Hunter.)

Triphenylphosphine, prepared by Dodonow and Medox's method (*Ber.*, 1928, **61**, 907) from phenylmagnesium bromide and phosphorus trichloride, was recrystallised three times from ethanol; m. p. 79° (uncorr.); Dodonow and Medox give m. p. 79·5°. Its oxide was prepared both by Sauvage's method (*Compt. rend.*, 1904, **139**, 675), *i.e.*, reaction of phenylmagnesium bromide with phosphorus oxychloride, and also by that of Michaelis and von Soden (*Annalen*, 1885, **229**, 306), *i.e.*, oxidation of triphenylphosphine with bromine and alkali. The product of the first method was recrystallised three times, that of the second method once, from benzene–ligroin. Both products had m. p. 159° (uncorr.); Sauvage gives m. p. 156°.

Tri-*p*-chlorophenylphosphine was very kindly provided by Dr. Mann, having been prepared by the method of Mann and Chaplin (J., 1937, 527); m. p. 104° (uncorr.) (Mann and Chaplin give m. p. 103°). Its oxide was made by bromine oxidation, as for the phenyl compound, and had m. p. 178° (uncorr.) after several recrystallisations from ethanol (Mann and Chaplin give m. p. 175°).

Triphenylphosphine–boron trichloride was prepared by the action of excess of the trichloride on the phosphine in benzene solution, there being an appreciable evolution of heat on reaction. After the excess of trichloride and some benzene had been distilled off, the product separated, and was recrystallised from benzene–ligroin under anhydrous conditions. It is readily hydrolysed by water to the phosphine and boric and hydrochloric acids; it fumes slightly in moist air, and is decomposed without melting above 100°. Hydrogen peroxide or bromine and alkali both attack it readily, yielding the phosphine oxide and hydrolysis products. Owing to this instability the analytical data are not very satisfactory (Found: C, 55·4; H, 4·1; Cl, 30·4. $C_{18}H_{15}Cl_3PB$ requires C, 56·9; H, 3·95; Cl, 28·0%).

Trimethylamine oxide was prepared by the method of Dunstan and Goulding (J., 1899, **75**, 1005). Its hydrate, recrystallised once from ethanol, had m. p. 96° (uncorr.) (Dunstan and Goulding, *ibid.*, p. 795, give m. p. 96°); it was converted into the oxide by heating to 110° in a vacuum, and purified by vacuum sublimation at 150°.

As the oxide is very hygroscopic, solutions for dipole measurements were prepared as follows. A suitable quantity of oxide was heated to 110° in a vacuum in an 8-mm. bore glass tube until thoroughly dried, and then sublimed up the tube. Dry air having been admitted, the tube was cooled, and the section containing the sublimate cut out and immediately closed with rubber bungs. After weighing, the solid was rapidly pushed with a glass rod into the dry benzene against a stream of dry air, and the tube weighed again before hydration of the residue could occur.

(Preparations by G. M. Phillips.)

Triphenylphosphine sulphide was prepared by the method of Michaelis and Gleichmann (*Ber.*, 1882, **15**, 803; cf. Michaelis and v. Soden, *ibid.*, p. 307) from triphenylphosphine and sulphur, the phosphine having been prepared as above (m. p. 81·5°, uncorr., after two recrystallisations, one with animal charcoal, from ethanol). The sulphide was recrystallised once from ethanol, giving m. p. 163° (uncorr.). Michaelis and v. Soden give m. p. 157·5° but Strecker and Grossmann (*Ber.*, 1916, **49**, 74) give 161°.

Triphenylphosphinephenylimine was prepared by the method of Staudinger and Meyer (*Helv. Chim. Acta*, 1919, **2**, 643) from triphenylphosphine and phenyl azide, the latter having been prepared as described by Dimroth (*Ber.*, 1902, **35**, 1032) and purified by distillation in a vacuum (b. p. 59°/15 mm.). After two recrystallisations from ether, the imine had m. p. 134° (uncorr.) (Staudinger and Meyer give m. p. 131—132°).

Trimethylphosphine–boron trichloride was prepared by distilling the phosphine off its silver iodide complex into an excess of boron trichloride, in a high vacuum. A white solid was formed immediately, the reaction being markedly exothermic. Excess of boron trichloride was distilled off, and the product purified by two vacuum sublimations (120°/0·5—1 mm.) and two recrystallisations from benzene [Found: C, 18·9; H, 4·7; Cl, 55·6 (by peroxide fusion). $C_3H_9Cl_3PB$ requires C, 18·6; H, 4·7; Cl, 55·0%]. The trimethylphosphine was prepared by the method of Hibbert (*Ber.*, 1906, **39**, 160) from methylmagnesium iodide and phosphorus trichloride, and was collected as the silver iodide complex (Mann, Wells, and Purdie, J., 1937, 1828).

The complex is a white solid, crystallising from benzene in fine needles. It is very stable to heat and to water: it sublimes at atmospheric pressure above 275° without any sign of decomposition, and is only very slowly hydrolysed by boiling with 5N-sodium hydroxide. Its solubility in benzene is low and it is, in general, very similar to its nitrogen analogue.

Diethyl ether–boron trifluoride was prepared from its components by the method of Gasselin (*Ann. Chim.*, 1894, **3**, 50) and purified by vacuum distillation; b. p. 60°/20 mm.

Trimethylamine–boron trifluoride was prepared by distilling the foregoing ether complex into a bulb containing excess of trimethylamine, in a vacuum apparatus (see Kraus and Brown, *J. Amer. Chem. Soc.*, 1929, **51**, 2690). The product, after three vacuum sublimations (60—70°/1—2 mm.), melted at 142—144° (corr.). After three further sublimations it melted at 146—146·5° (corr.) (Burg and Green, *J. Amer. Chem. Soc.*, 1943, **65**, 1838, give 139—147°) (Found: C, 28·5; H, 7·2; N, 11·1. Calc. for $C_2H_9NF_3B$: C, 28·4; H, 7·15; N, 11·0%). It is a white crystalline substance forming fine needles when sublimed slowly. When pure, the solid is stable and may be kept in a well-corked tube. When impure, it slowly turns brown, as did the triethylamine compound described by Kraus and Brown. It hydrolyses readily when in solution, and so is better purified by sublimation than by recrystallisation. Its solubility in both benzene and ether is rather low.

Trimethylamine–boron trichloride (Wiberg and Sütterlin, *Z. anorg. Chem.*, 1931, **202**, 35) was prepared by the same method as the triphenylphosphine compound. Trimethylamine, generated from sufficient hydrochloride to give an excess, was absorbed in benzene, and the trichloride was then distilled in. The product was recrystallised twice from benzene to a constant m. p. 245° (corr.; slight decomp.). Wiberg and Sütterlin give m. p. 243—244° without decomposition.

Diisobutyl sulphide–boron trichloride was prepared by the reaction of excess of the trichloride with the sulphide in ligroin (b. p. 40—60°) solution. The sulphide was prepared by the method of Beckmann (*J. pr. Chem.*, 1878, **17**, 445) as modified by Hammick and Williams (J., 1938, 211), and the trichloride was a commercial specimen purified in a MacGillivray–Podbielniak vacuum-jacketed fractionating column. After removal of the ligroin, the product was distilled in a vacuum (b. p. 87°/1—2 mm.). The complex is very unstable to heat and moisture. It fumes strongly in moist air; and a considerable black residue is left on vacuum distillation owing to thermal decomposition. It is a white solid (m. p. with marked decomposition *ca.* 50°) which rapidly becomes pink on standing. It is very soluble in light petroleum and in benzene. Owing to the instability the analytical results are very unsatisfactory (Found : C, 39·1; H, 7·0. $C_8H_{18}Cl_3SB$ requires C, 36·45; H, 6·9%).

This substance proved unsuitable for accurate electric dipole moment measurements; but since it seemed possible that the diethyl compound would distil with less decomposition and, if it were a liquid, be easier to manipulate, it was prepared.

Diethyl sulphide–boron trichloride, prepared just as was the di*iso*butyl compound, was purified by two distillations in a vacuum. It is a colourless, slightly oily liquid, b. p. 90°/1—2 mm. It was analysed by hydrolysis and silver titration of the chloride ion (Found : Cl, 51·6, 51·3, 51·4. $C_4H_{10}Cl_3SB$ requires Cl, 51·3%). Although it fumes slightly in moist air, is vigorously hydrolysed by water, and leaves a very slight residue on vacuum distillation, it is very much more stable both to heat and to moisture than is the di*iso*butyl compound and can be kept for a week in a well-stoppered tube before decomposition is significant. It is completely miscible with dry benzene or ligroin.

Fluorenyl-9-dimethylsulphonium bromide was prepared from 9-bromofluorene and methyl sulphide as described by Ingold and Jessop (J., 1930, 713). The 9-bromofluorene was obtained from fluorene by the stages, fluorenone (Huntress, Hershberg, and Cliff, *J. Amer. Chem. Soc.*, 1931, **53**, 2720), 9-hydroxyfluorene (Werner and Grob, *Ber.*, 1904, **37**, 2895), 9-bromofluorene (Ingold and Jessop, J., 1929, 2357).

Dimethylsulphonium-9-fluorenylidide was precipitated from the aqueous solution of the sulphonium bromide with alkali on the day it was required for use, washed with alcohol and ether, and dried in a vacuum for about 3 hours. The m. p. was 126—127° with decomposition after melting, but Ingold and Jessop recorded 70—75° with decomposition on rapid heating. It seems possible that this decomposition was caused by occluded alkali; for, although most of our samples, which were precipitated from very dilute solutions (0·25%), gave the high m. p., yet one sample, precipitated from a 2% solution, melted at 81—86°. A sample, m. p. 127—129°, was analysed (Found : C, 78·4; H, 5·9. Calc. for $C_{15}H_{14}S$: C, 79·65; H, 6·2%). As methyl sulphide is readily lost above the m. p., these results were accepted as adequate.

Because of the instability of the compound in solution, Ingold and Jessop's method of measuring the molecular weight cryoscopically was adapted to the dipole moment measurement; *i.e.*, dielectric constant was plotted against time, and the curve extrapolated to zero time. The density was shown not to vary significantly with time.

Physical Measurements.—Electric dipole moments were determined from measurements of the dielectric constant, refractive index, and density of benzene solutions at the same temperature. Dielectric constants were determined by a heterodyne beat method using an apparatus and a technique essentially the same as those described before (Sutton, *Proc. Roy. Soc.*, 1931, *A*, **133**, 668; Hampson, Farmer, and Sutton, *loc. cit.*), the solution condenser being similar to that described by H. O. Jenkins and Sutton (J., 1935, 609).

Densities were determined with a 10-ml. Sprengel–Ostwald pyknometer.

Refractive indices were measured relative to the solvent with a Pulfrich refractometer fitted with a divided cell, the mercury green line (5461 A.) being used for illumination.

For several reasons, including the instability and the low solubility of some of the compounds, it was not always possible to obtain molecular refractivities of the usual accuracy; so for these substances calculated values were used. Fortunately, since the moments were large, errors of a few c.c. in this quantity were immaterial. The following values of atomic refractivities were used in the calculations. From tables : C, 2·43; H, 1·11; CH_2, 4·69; O^{II}, 1·65; N^{III}, 2·89; Cl, 6·01; F, 0·99; S^{II}, 7·77; P, 9·09; double bond 1·69 c.c. From other results in this paper : increase on co-ordination of BCl_3, 18 c.c. (from $PPh_3,BCl_3 - PPh_3 = 18$, and $SEt_2,BCl_3 - SEt_2 = 18$); increase on co-ordination of BF_3, 2·7 c.c. (from $BCl_3 + 3F - 3Cl = 3$, and $OEt_2,BF_3 - Et_2O = 2·4$).

The dielectric constant of pure dry benzene was taken to be 2·2727 at 25° (Hartshorn and Oliver, *Proc. Roy. Soc.*, 1929, *A*, **123**, 664; Sugden, J., 1933, 768), that of dry air 1·0000. The refractive index of pure dry benzene at 25° was taken to be 2·25714.

Atom polarisations were allowed for by adding 5% to the electron polarisation calculated for the wave-length 5461 A.

The usual symbols are used in the tables; n refers to λ 5461 A., and the subscripts " soln." and " vap." are used when moments in solution and those measured in the vapour phase (or those approximately corrected for solvent effect) need to be distinguished.

Results.—All measurements are in benzene solution at 25°. Moments are expressed in Debye units (1 D. = 10^{-18} e.s.u.).

(Measurements by J. S. Hunter.)

Triphenylphosphine.

f_2.	$d_4^{25°}$.	ε.	n^2.	P_2.	$_ED_2$.	f_2.	$d_4^{25°}$.	ε.	n^2.	P_2.	$_ED_2$.
0·00000	0·8740	2·2727	2·25714	—	—	0·01951	0·8857	2·3584	2·2574	136·9	93·84
0·00661	0·8776	2·3012	2·2568	136·9	94·04	0·03213	0·8933	2·4154	2·2580	136·4	93·21
0·01053	0·8810	2·3204	2·2573	138·4	93·31						

$_\infty P_2 = 138·4$; $_ED_2 = 93·6$; $_AP_2 = 4·7$; $_OP_2 = 40·1$ c.c.; $\mu = 1·39 \pm 0·04$ D.

Bergmann and Schütz (*Z. physikal. Chem.*, 1932, *B*, **19**, 401) report 1·45 D. for the moment of this substance (m. p. given as 78°).

Triphenylphosphine oxide.

0·00000	0·8738	2·2727	2·2571	—	—	0·01892	0·8903	2·8359	2·2750	468·0	90·36
0·00630	0·8792	2·4534	2·2662	474·4	91·02	0·02836	0·8980	3·1337	2·2805	466·3	90·33
0·01325	0·8853	2·6653	2·2683	472·9	90·81						

$_\infty P_2 = 477$; $_ED_2 = 91$; $_AP_2 = 5$; $_OP_2 = 381$ c.c.; $\mu = 4·28 \pm 0·02$ D.

Jensen (*Z. anorg. Chem.*, 1943, **250**, 268) reports $\mu = 4·31$ D.

Tri-p-chlorophenylphosphine.

f_2.	$d_4^{25°}$.	ε.	n^2.	P_2.	$_ED_2$.	f_2.	$d_4^{25°}$.	ε.	n^2.	P_2.	$_ED_2$.
0·00000	0·8742	2·2727	2·2571	—	—	0·01381	0·8931	2·3028	2·2639	113·6	100·43
0·00759	0·8848	2·2894	2·2636	114·3	100·61	0·02374	0·9059	2·3244	2·2643	113·3	100·36

$_\infty P_2 = 114·4$; $_ED_2 = 100·5$; $_AP_2 = 5$; $_OP_2 = 8·9$ c.c.; $\mu = 0·65 \pm 0·07$ D.

Tri-p-chlorophenylphosphine oxide.

0·00000	0·8742	2·2727	2·2571	—	—	0·01463	0·8974	2·4723	2·2652	278·2	97·84
0·00609	0·8842	2·3559	2·2629	277·6	98·03	0·02239	0·9103	2·5819	2·2662	275·9	97·94
0·00719	0·8856	2·3716	2·2639	279·5	97·91						

$P_2 = 281$; $_ED_2 = 98$; $_AP_2 = 5$; $_OP_2 = 178$ c.c.; $\mu = 2·93 \pm 0·03$ D.

Triphenylphosphine–boron trichloride.

0·00000	0·8741	2·2727	2·2571	—	—	0·00526	0·8771	2·8104	2·2781	1132	111·6
0·00253	0·8754	2·4458	2·2751	1112	112·5	0·00971	0·8796	3·1620	2·2801	1094	111·2

$_\infty P_2 = 1140$; $_ED_2 = 112$; $_AP_2 = 6$; $_OP_2 = 1022$ c.c.; $\mu = 7·01 \pm 0·06$ D.

(Measurement by N. J. Leonard.)

Trimethylamine oxide.

0·0000	0·8740	2·2727	—	—	—	0·000351	0·8740*	2·28390	—	490·8	—
0·000295	0·8740*	2·28322	—	545·9	—	0·000450	0·8740*	2·28821	—	529·6	—

* The densities were all taken to be the same as that of the pure solvent, since it was found in some preliminary experiments that the differences are inside the experimental error in the case of such dilute solutions.

$_\infty P_2 = 522 \pm 30$; $_ED_2 = 30$; $_OP_2 = 492 \pm 30$ c.c.; $\mu = 4·87 \pm 0·15$ D.

Linton (*J. Amer. Chem. Soc.*, 1940, **62**, 1945) reports values for the moment of this substance of 5·04 D. in dioxan solution at 25°, and 5·02 D. in benzene solution at 45°. Since these solutions are more concentrated than those above, his values are probably more accurate than ours.

(Measurements by G. M. Phillips.)

Triphenylphosphine sulphide.

0·00000	0·8729	2·2727	—	—	—	0·00465	0·8773	2·4244	—	537·8	—
0·00112	0·8741	2·3107	—	564·2	—	0·00850	0·8809	2·5588	—	544·9	—
0·00208	0·8747	2·3426	—	562·5	—						

$_\infty P_2 = 568$; $_AP_2 = 5$; $_ED_2 = 97$ (calc. from $PPh_3O + S^{II} - O^{II}$); $_OP_2 = 466$ c.c.; $\mu = 4·73 \pm 0·02$ D.

Jensen (*loc. cit.*) reports $\mu = 4·74$ D.

Triphenylphosphinephenylimine.

0·00000	0·8737	2·2727	—	—	—	0·00365	0·8802	2·3871	—	515·5	—
0·000938	0·8753	2·3023	—	528·7	—	0·00724	0·8864	2·4993	—	507·0	—
0·00180	0·8770	2·3290	—	516·9	—						

$P_2 = 525$; $_AP_2 = 6$; $_ED_2 = 117$ (calc. from $PPh_3O + NPh - O$); $_OP_2 = 402$ c.c.; $\mu = 4·40 \pm 0·03$ D.

Jensen (*loc. cit.*) reports $\mu = 4·45$ D.

Trimethylphosphine–boron trichloride.

0·00000	0·8740	2·2727	—	—	—	0·00174	0·8753	2·3931	—	1032	—
0·00101	0·8748	2·3434	—	1049	—	0·00241	0·8759	2·4388	—	1017	—

The low solubility prevented direct measurements of $_ED_2$. By subtracting the normal values for $3(C_6H_5)$ from the observed value for PPh_3,BCl_3 and adding the normal values for $3(CH_3)$ a value of 54 c.c. is obtained. This is 10 c.c higher than the sum of the atomic refractivities for $P(CH_3)_3$ plus 18 c.c. for BCl_3. The anomaly is the same as that between the observed and calculated values for PPh_3 itself, and so seems to be associated with the presence of phenyl groups. Therefore the second value, 44 c.c., was taken.

$_\infty P_2 = 1070$; $_ED_2 = 44$; $_AP_2 = 2$; $_OP_2 = 1024$ c.c.; $\mu = 7·03 \pm 0·01$ D.

Trimethylamine–boron trifluoride.

0·00000	0·8737	2·2727	—	—	—	0·00171	0·8740	2·3484	—	676·2	—
0·00091	0·8739	2·3144	—	700·5	—	0·00213	0·8741	2·3684	—	683·3	—
0·00115	0·8739	2·3251	—	697·6	—						

$_\infty P_2 = 713$; $_AP_2 = 1$; $_ED_2 = 23$ (calc. from sum of atomic refractivities + 2·7 c.c. for BF_3); $_OP_2 = 689$ c.c.; $\mu = 5·76 \pm 0·02$ D.

Bright and Fernelius (*J. Amer. Chem. Soc.*, 1943, **65**, 735) show that this substance is associated in benzene solution. Their weakest solution was, however, stronger than the strongest of those above; and, in any case, the effect of association should be eliminated by extrapolating the polarisation to infinite dilution.

Trimethylamine–boron trichloride.

0·00000	0·8732	2·2727	—	—	—	0·000356	0·8734	2·2920	—	829·4	—
0·000283	0·8734	2·2883	—	841·3	—	0·001003	0·8739	2·3285	—	845·5	—
0·000545	0·8736	2·3028	—	843·0	—	0·001783	0·8746	2·3729	—	842·4	—

$_\infty P_2 = 846$; $_AP_2 = 2$; $_ED_2 = 38$ (calc. as sum of atomic refractivities + 18 c.c. for BCl_3); $_OP_2 = 806$ c.c.; $\mu = 6·23 \pm 0·02$ D.

Diethyl ether–boron trifluoride.

f_2.	$d_4^{25°}$.	ε.	n^2.	P_2.	$_RP_2$.	f_2.	$d_4^{25°}$.	ε.	n^2.	P_2.	$_RP_2$.
0·00000	0·8740	2·2727	2·2571	—	—	0·00000	0·8735	2·2727	—	—	—
0·01408	0·8801	2·8602	2·2466	575·4	23·59	0·01092	0·8772	2·7021	—	564·3	—
0·02529	0·8843	3·2708	2·2406	509·1	25·67	0·02148	0·8814	3·1261	—	526·9	—

$_\infty P_2 = 608$; $_RP_2 = 25$; $_AP_2 = 1$; $_OP_2 = 582$ c.c.; $\mu = 5{\cdot}29 \pm 0{\cdot}03$ D.

Laubengayer and Finlay (*J. Amer. Chem. Soc.*, 1943, **65**, 884) find the moment of this substance to be $4{\cdot}35 \pm 0{\cdot}12$ D.; but their solutions were evidently partly hydrolysed, so we consider our result to be the more reliable.

Diethyl sulphide–boron trichloride.

0·00000	0·8733	2·2727	2·2571	—	—	0·01088	0·8824	2·8718	2·2583	758·9	45·95
0·00500	0·8774	2·5371	2·2580	779·2	47·65	0·01778	0·8877	3·2926	2·2601	733·9	47·70

$_\infty P_2 = 797$; $_RP_2 = 47$; $_AP_2 = 2$; $_OP_2 = 748$ c.c.; $\mu = 6{\cdot}00 \pm 0{\cdot}01$ D.

Dimethylsulphonium-9-fluorenylidide.

Variation of dielectric constant with time.

f_2, 0·000364.		f_2, 0·000629.		f_2, 0·000735.		f_2, 0·001509.	
Time, mins.	ε.	Time, mins.	ε.	Time, mins.	ε.	Time, mins.	ε.
11·75	2·2865	25·75	2·2905	18	2·2991	22·5	2·3154
17·25	2·2842	33·25	2·2865	23·5	2·2962	27·25	2·3108
24·25	2·2824	40·75	2·2838	29	2·2937	33·25	2·3074
31·5	2·2809	52	2·2809	35·5	2·2911	38	2·3051
42·75	2·2801	57·5	2·2803	40·5	2·2892	43·75	2·3028
53·75	2·2800	70	2·2794	53·75	2·2850	49·5	2·3009
						55·75	2·2990

Density, dielectric constant, and polarisation as a function of molar fraction.

f_2.	$d_4^{25°}$	ε_{zero}, measd.	ε_{zero}, mean.	P_2.
0·00000	0·8735	2·2727	2·2727	—
0·000505	0·8738	—	—	—
0·000889	0·8743	—	—	—
0·000364	0·8738 *	2·2936 ± 0·0004	2·2934	882 †
0·000629	0·8740 *	2·3116 ± 0·0010	2·3081	871 †
0·000735	0·8741 *	2·3147 ± 0·0010	2·3141	872 †
0·001509	0·8747 *	2·3519 ± 0·0050	2·3580	868 †

$_\infty P_2 = 876$; $_RP_2 = 70$ (calc. as sum of atomic refractivities, no allowance being made for the C←S link); $_AP_2 = 4$; $_OP_2 = 802$ c.c. (estimated error ± 50 c.c.); $\mu = 6{\cdot}2 \pm 0{\cdot}2$ D.

*† The values of dielectric constant at zero time, obtained by extrapolation, were plotted against mole-fraction, and the best mean curve drawn. Points from this (ε_{zero} mean) were then used for calculating the total polarisation (†) at the several mole-fractions. Since densities had to be determined in separate runs, interpolated values (*) were used in these calculations.

Discussion.

(Throughout this discussion, " D." is omitted after dipole moments.)

The most obvious way in which to analyse the experimental data would be to derive the dipole moments of the particular bonds in which we are interested and to compare them. In practice, however, this cannot be done at all accurately when the bonds are in such complicated molecules, because of the inadequacy of the assumptions which have to be made (cf. Sutton, *Ann. Reports*, 1940, **37**, 54); so the argument would be weakened by the uncertainties thus introduced. Initially, therefore, it is better to follow a simpler procedure, introducing as few assumptions as possible. Hence, we propose first to compare, not the moments of the bonds themselves, but the apparent vector changes of moment which accompany their formation, to do this for a series of related compounds, and to look for irregularities which might reveal changes in bond type.

Accordingly, we have calculated the changes which occur when amines, phosphines, ethers, or sulphides add on oxygen, sulphur, or boron halides. They are the vectors which must be considered to arise along the conjectured directions of the new bonds, if we suppose that when the latter are formed the moment of the donor molecule remains unchanged; this assumption is probably inaccurate, but the comparisons in related series should still be valid.

For symmetrical amines or phosphines, the new bond is along the axis of symmetry; so the required vector is simply the algebraic difference of the moments of the donor molecule and of the complex. To calculate the vector change on formation of ether or thioether complexes, we may reasonably assume the bonds to radiate from a donor atom along the axes of a regular tetrahedron, so the new bond makes an angle of 125° 16′ with the resultant of the other two.

The moments used in these calculations are listed below. It is supposed that in the amines, phosphines, ethers, and sulphides the negative end of the dipole is *away from* the carbon atoms. The moments of their oxides, sulphides, and boron complexes are supposed to be in the same general direction, *i.e.*, with the negative end towards the added atom or group. The values quoted are mostly observed in benzene solution: in some cases the value in the gas phase is known and is given also, with a subscript (*g*) to distinguish it. Numbers in parenthesis in the list of sources relate to the list in " A Table of Dipole Moments " (*Trans. Faraday Soc.*, 1934, **30**).

Substance.	Moment.	Source.
Trimethylamine	0·65$_9$	Groves and Sugden, J., 1937, 1779.
	0·74	Estimated.
Triethylamine	0·69$_9$	Higasi, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1937, **31**, 311.
	0·79	
Trimethylamine oxide	(4·87)	Present work.
	5·03	Linton, *J. Amer. Chem. Soc.*, 1940, **62**, 1945.
,, $-BCl_3$	6·23	Present work.
,, $-BF_3$	5·76	,,
Ethylamine	0·99	Ghosh (134).
,, $-AlCl_3$	6·94	Ulich (197).
Trimethylphosphine	(1·2)	Estimated.
,, $-BCl_3$	7·03	Present work.
β-Bistriethylphosphine platinochloride	10·7	Jensen, *Z. anorg. Chem.*, 1936, **229**, 225.
Triphenylphosphine	1·39	Present work.
,, oxide	4·28	,, ; Jensen, *ibid.*, 1943, **250**, 268.
,, sulphide	4·73	,, ,, ,, ,,.
,, $-BCl_3$	7·01	,,
,, selenide	4·83	Jensen (*loc. cit.*, 1943).
Triethylamine	1	Estimated.
β-Bistriethylarsine platinochloride	10·5	Jensen (*loc. cit.*, 1936).
Triphenylarsine	1·07	Bergmann (226).
,, oxide	5·50	Jensen (*loc. cit.*, 1943).
Triphenylstibine	0·57	Bergmann (226).
,, oxide	~2·3	Jensen (*loc. cit.*, 1943).
,, sulphide	5·40	,, ,,
β-Triphenylstibine platinochloride	9·3	Jensen (*loc. cit.*, 1936).
Diethyl ether	1·14	"A Table of Dipole Moments," *loc. cit.*, various authors.
	1·18$_9$	Groves and Sugden, *loc. cit.*
,, $-BCl_3$	5·98	Ulich (197).
,, $-BF_3$	5·29	Present work.
	(4·92)	Laubengayer and Finlay, *loc. cit.*
Methyl sulphide	1·40	Partington (147).
Dimethylsulphone	4·44$_9$	Coop and Sutton, *Trans. Faraday Soc.*, 1939, **35**, 495.
Dimethylsulphonium-9-fluorenylidide	6·2	Present work.
Ethyl sulphide	1·58	Smyth (260).
,, $-BCl_3$	6·00	Present work.
β-Bisdiethylsulphide platinochloride	9·5	Jensen, *Z. anorg. Chem.*, 1935, **225**, 97.
Diethylsulphone	4·41	Sutton (257).
*iso*Butyl sulphide	1·58	Williams, "A Table of Dipole Moments," *loc. cit.*
,, sulphoxide	3·90	Hammick and Williams, J., 1938, 211.
Phenyl sulphide	1·50	Hampson (269).
Diphenyl sulphoxide	4·00	,,
Diphenylsulphone	5·05	de Vries (149).
Phenyl selenide	1·38	Bergmann (107).
Diphenyl selenoxide	4·44	Jensen (*loc. cit.*, 1943).
Phenyl telluride	1·13	Bergmann (107).
pp'-Ditolyl telluroxide	3·93	Jensen (*loc. cit.*, 1943).

The calculated vector changes are set out on p. 155. The plain figures are calculated from the above data on the assumptions already given, without any corrections for solvent effect or for mesomeric moment changes. The latter can arise only in the phenyl compounds, while the former, according to Frank's theory of the solvent effect (*Proc. Roy. Soc.*, 1935, **152**, 171), is unlikely to be important for most of the substances concerned. For triphenylphosphine, its oxide and sulphide, however, it seems desirable to allow for these factors, so corrected values are given in italics, the methods of correction being indicated by notes. These should be more comparable with the uncorrected values for the other substances; but it will be seen that the corrections do not affect the main conclusions. Values deemed to be of doubtful accuracy are in parenthesis.

From this table it will be observed that the vector changes, to be referred to hereinafter as $\Delta\mu_{XY}$, are not very different for the formation of the $\geqslant N\rightarrow O$, $\geqslant N\rightarrow BCl_3$, and $\geqslant N\rightarrow BF_3$ groupings, ranging from 4·25 to 5·5; and that $\Delta\mu_{P\rightarrow BCl_3}$ is about the same as $\Delta\mu_{N\rightarrow BCl_3}$. Assuming that the simple relation $\Delta\mu_{N\rightarrow O}/\Delta\mu_{P\rightarrow O} = \Delta\mu_{N\rightarrow BCl_3}/\Delta\mu_{P\rightarrow BCl_3}$ holds, we should expect that $\Delta\mu_{P\rightarrow O}$ would be about 4·25; but $\Delta\mu_{PO}$ is only *ca.* 2·7, so PO appears not to be P→O.

For the $\geqslant PS$ and the $\geqslant PSe$ link the argument is similar, though the data are less complete. From the values for $\Delta\mu_{N\rightarrow O}$, $\Delta\mu_{N\rightarrow BCl_3}$, and $\Delta\mu_{P\rightarrow BCl_3}$ we should expect the values of $\Delta\mu_{P\rightarrow S}$ and $\Delta\mu_{P\rightarrow Se}$ to be at least 4·25; whereas the values of $\Delta\mu_{PS}$ and $\Delta\mu_{PSe}$ are only 3·1 and 3·2, respectively. It would be better to use values for $\Delta\mu_{P\rightarrow AlCl_3}$ and $\Delta\mu_{P\rightarrow GaCl_3}$ to derive those for $\Delta\mu_{P\rightarrow S}$ and $\Delta\mu_{P\rightarrow Se}$, through relations of the type $\Delta\mu_{N\rightarrow O}/\Delta\mu_{P\rightarrow S} = \Delta\mu_{N\rightarrow BCl_3}/\Delta\mu_{P\rightarrow AlCl_3}$, in an attempt to allow for the effect of the greater radii of sulphur and of selenium, which should make the values expected larger than 4·25; but these data are not available. A rough value of $\Delta\mu_{P\rightarrow PtCl_3}$ is 6·4; which is, as anticipated, considerably larger than $\Delta\mu_{P\rightarrow BCl_3}$.

The values of $\Delta\mu_{AsO}$ and of $\Delta\mu_{SbS}$ are about the same as $\Delta\mu_{N\rightarrow O}$, though they are still considerably less than those for $\Delta\mu_{As\rightarrow PtCl_3}$ and $\Delta\mu_{Sb\rightarrow PtCl_3}$; so no very definite conclusions can be drawn about these bonds from existing data. $\Delta\mu_{SbO}$ is so irregular that one would like to see the value confirmed.

The above argument cannot be applied in full to the case of the SO bond, because there is no direct determination of the vector change when ethereal oxygen co-ordinates oxygen, *i.e.*, $\Delta\mu_{O\rightarrow O}$; but, assuming that

TABLE II.

Vector Changes, $\Delta\mu_{XY}$.

>NO 4·25^{Me_2}		>N,BCl$_3$ 5·50^{Me_2}		>N,BF$_3$ 5·02^{Me_2}	>N,AlCl$_3$ (5·9)^{EtH_2}	
>PO 2·89^{Ph_3} *2·66*		>P,BCl$_3$ 5·62^{Ph_3} *5·39*	(5·8)^{Me_2}			
	>PS 3·36^{Ph_3} *3·11*	>PSe 3·44^{Ph_3} *3·21*				>P,PtCl$_2$ (6·4)^{Et_2}
>AsO 4·43^{Ph_3} *4·14*						>As,PtCl$_2$ (6·4)^{Et_2}
>SbO ((1·7))^{Ph_3}	>SbS 4·83^{Ph_3} *4·46*					>Sb,PtCl$_2$ (6·12)^{Ph_3}
>OO [4·05] >SO 2·5—3·0 >SeO (3·06)^{Ph_2} >TeO (2·3)$^{(PhMe)_2}$		>O,BCl$_3$ 5·29^{Et_2} >S,BCl$_3$ 4·98^{Et_2}		>O,BF$_3$ 4·58^{Et_2} >S,C$_{12}$H$_8$ (5·3)^{Me_2}		>S,PtCl$_2$ (5·3)^{Et_2}

Notes.—Correction for PO: Gas-phase moment for triphenylphosphine estimated to be 1·12 D.; for the oxide, μ(g) estimated equal to μ(soln.); mesomeric difference in triphenylphosphine and its oxide supposed to be −0·5 D.

Correction for PS: As for PO.

Correction for P,BCl$_3$: μ(g) for triphenylphosphine estd. 1·12 D.; mesomeric moment difference in triphenylphosphine and the BCl$_3$ complex supposed to be −0·5 D.; μ(g) for the latter estd. equal to μ(soln.).

The superscript signs—Ph_3, Me_2, etc.—show that the values so distinguished are derived from data for the triphenyl, dimethyl, etc., compounds.

The values of the PO and the PS vector changes from the data for phosphorus trichloride, phosphoryl chloride, and thiophosphoryl chloride are 3·5 and 2·4, respectively. These are deemed less reliable, because of the greater probability of a considerable mutual alteration of moments by induction. The value from the data for *pp'p''*-trichlorophenylphosphine and its oxide is ambiguous, being 3·6 or 2·3 according to which way round the moment of the former is supposed to be.

the difference between $\Delta\mu_{O\rightarrow BCl_3}$ and the hypothetical $\Delta\mu_{O\rightarrow O}$ is the same as that between $\Delta\mu_{N\rightarrow BCl_3}$ and $\Delta\mu_{N\rightarrow O}$, we find $\Delta\mu_{O\rightarrow O} = 4{\cdot}04$; or, assuming that $\Delta\mu_{O\rightarrow O}/\Delta\mu_{N\rightarrow O} = \Delta\mu_{O\rightarrow BCl_3}/\Delta\mu_{N\rightarrow BCl_3}$, we find $\Delta\mu_{O\rightarrow O} = 4{\cdot}09$. A value 4·05 is therefore taken. Thence we estimate $\Delta\mu_{S\rightarrow O}$ to be 3·8, whereas $\Delta\mu_{SO}$ is 2·5—3·0. $\Delta\mu_{SeO}$ and $\Delta\mu_{TeO}$ are also less than the estimated $\Delta\mu_{S\rightarrow O}$. $\Delta\mu_{S,C_{12}H_8}$ has, however, the high value to be expected if the sulphur–carbon link were a dative bond, as it is in Ingold and Jessop's formulation (J., 1930, 713).

From this simple consideration of magnitudes of moments changes we conclude that the PO, PS, PSe, SO, SeO, and TeO oxy-bonds are not pure co-ordinate links (cf. Smyth, *J. Amer. Chem. Soc.*, 1938, **60**, 183); but the differences between the observed and the calculated values are not always large. This conclusion becomes much more definite, however, when we consider what the observed moments would mean if we supposed that the bonds were, nevertheless, co-ordinate links.

We must first calculate values for the moments of all the relevant bonds, bearing in mind that this can be done only very roughly. If we ignore the possible effects of mutual induction, these bond moments are either, for the links to oxygen, the same as the vector changes given above, or, for the links to boron, they can be taken as the vector changes less the moments of the BCl$_3$ or BF$_3$ parts which are assumed to be equal to those of chloroform (1·2 D.) and of fluoroform (1·6 D.) respectively. The following are the values obtained:

$\mu_{NO} = 4{\cdot}25$ D.	$\mu_{NB} = 4{\cdot}3, 3{\cdot}4$ D.	
$\mu_{PO} = 2{\cdot}66$	$\mu_{PB} = 4{\cdot}2, 4{\cdot}6$	
$\mu_{PS} = 3{\cdot}11$		
	$\mu_{OB} = 4{\cdot}1, 3{\cdot}0$	
$\mu_{SO} = 2{\cdot}5$—$3{\cdot}0$	$\mu_{SB} = 3{\cdot}78$	$\mu_{SC} = 5{\cdot}0$

We then calculate the degree of sharing of the bonding electrons. If they were symmetrically shared between the donor and the acceptor atoms, the bond moment would be $4{\cdot}80l$ (l being the bond length in A.). If the moment is actually $4{\cdot}80lx$, then we may suppose that the centroid of the bonding electrons is distant from the donor atom only a fraction $x/2$ of the bond length. By taking the observed interatomic distances for the bonds of disputed character (see Table I),* and observed or estimated ones for the definite co-ordinate links (using the Pauling radii, $r_N = 0{\cdot}70$, $r_O = 0{\cdot}66$, $r_S = 1{\cdot}04$, $r_P = 1{\cdot}10$ A., and the Bauer and Beach radius for boron, 0·85 A., since these give good results for known cases, cf. p. 148), we can calculate the values of x to be the following:

NO 0·65	NB 0·58—0·46	
PO 0·36	PB 0·45—0·49	
PS 0·33		
	OB 0·56—0·41	
SO 0·36—0·44	SB 0·42	SC 0·575

* These calculations cannot be done for such bonds when the distance has not been observed, since to use lengths calculated for co-ordinate links, in the case of these bonds of unknown character, would be to beg the question.

In no case is $\varkappa$ unity. The values for the PO, PS, and SO bonds show the same irregularities as did the vector changes.

In the limit, when a " co-ordinate link " has no moment and $\varkappa$ is therefore zero, there is no bond; so it seems reasonable to suppose that the smaller $\varkappa$ is, the weaker is the co-ordinate link.* Hence we should expect that if the PO, PS, and SO bonds were co-ordinate links they would be weak ones, weaker than the others.† We shall show, however, that actually they appear to be much the stronger.

This is indicated qualitatively by the facts that amine oxides have to be made by the action of strong oxygenating agents on amines, and can be reduced back by zinc dust and acid or alkali (" Beilstein," IV, p. 49), whereas the phosphine oxides are formed very readily, sometimes by aerial oxidation, and cannot be reduced back at all easily. Similarly, the pentoxide of phosphorus is much more stable relative to the trioxide than nitrogen pentoxide is to the lower oxides.

From existing thermal data (see Bichowsky and Rossini, " The Thermochemistry of Chemical Substances," New York, 1936) the heat of the reaction $PCl_3(g) + O(g) \longrightarrow POCl_3(g)$, *i.e.*, the apparent heat of formation from the atoms (H_a) of the PO bond, is calculated to be 127·5 kg.-cals./g.-mol. One of 138 kg.-cals./g.-mol. is got from the experimental value of H_a for phosphoric oxide, P_4O_{10}, and an estimated one for the oxide P_4O_6; the latter being taken as that of twelve P–O bonds, the values for which are calculated by Pauling's method (*op. cit.*, Chap. II), from the experimental H_a values for the P–P and the O–O bond and the difference of electronegativity co-ordinates, to be 72·1 kg.-cals./g.-mol each. Similarly, from data for thionyl chloride and sulphuryl chloride a value of 102·6 kg.-cals./g.-mol. is found for H_a of the SO bond. Furthermore, from data for chlorine heptoxide (Goodeve and Marsh, J., 1937, 1161) and monoxide (Bichowsky and Rossini, *op. cit.*) a value of 52 kg.-cals./g.-mol. for the oxy-bond ClO is found. Thus, all three bonds are strong, the first two especially.‡

From the data for nitrogen trioxide and pentoxide and the heat of atomisation of oxygen (Bichowsky and Rossini, *op. cit.*), the apparent heat of formation of the N→O link is 68·8 kg.-cals./g.-mol.; while from those for ethyl nitrite and nitrate it is 66·6. These values include an unknown resonance energy which may be as much as 20 kg.-cals. It is therefore obvious that the PO and the SO bond, far from being weaker, are much stronger.

We may also compare the experimental values for H_a(PO) and H_a(SO) with those estimated for H_a(P→O) and H_a(S→O) by a process like that used for getting the theoretical vector changes of moment, *i.e.*, by supposing that $H_a(N\rightarrow O)/H_a(P\rightarrow O) = H_a(N\rightarrow B \text{ or Al})/H_a(P\rightarrow B \text{ or Al})$. H_a(S→O) can be obtained similarly. We now need H_a(N→B or Al), H_a(P→B or Al), and H_a(S→B or Al).

The apparent heat of formation of a co-ordinate link in a complex is the same as the heat of reaction of the donor and acceptor molecules. Such values for the combination of amines with boron compounds have been determined by Schlesinger, Flodin, and Burg (*J. Amer. Chem. Soc.*, 1939, **61**, 1079) and by Burg and Green (*ibid.*, 1943, **65**, 735). They find the following values of $-\Delta H$: NMe_3,BMe_3 (g), 14 kg.-cals./g.-mol.; NMe_3,BMe_2F (g), 18·3; $NMe_3,BMeF_2$ (g), 23·1. $-\Delta H$ could not be obtained for NMe_3,BF_3 by their method (variation of the degree of dissociation of the vapour with temperature), but a value of 28·5 is found by extrapolating the above data. Bauer, Finlay, and Laubengayer (*loc. cit.*) quote a value of 9 ± 1 for $-\Delta H$ of NH_3,BMe_3 (g), got from the data of Stock and Ziedler (*Ber.*, 1921, **54**, 531), one of 51 for C_5H_5N,BF_3 (g) (van der Meulen and Heller, *J. Amer. Chem. Soc.*, 1932, **54**, 4404), and they report that $-\Delta H$ for NH_3,BF_3 (solid) is 42. The heat of the reaction NH_3 (g) + $AlCl_3$ (g) ⟶ $NH_3,AlCl_3$ (cryst.) can be calculated from the tabulated data (Bichowsky and Rossini, *op. cit.*) to be 72 kg.-cals./g.-mol. Laubengayer and Finlay (*loc. cit.*) find $-\Delta H$ for the gaseous dimethyl and diethyl etherates of boron trifluoride to be $13·9\pm0·7$ and $12·5\pm1·0$ kg.-cals./g.-mol., respectively.

No data exist for the heats of formation of phosphine complexes with boron compounds, but $-\Delta H$ for PH_3 (g) + $AlCl_3$ (g) ⟶ $PH_3,AlCl_3$ (cryst.) is 43·7 kg.-cals./g.-mol., *i.e.*, considerably less than for the corresponding amine, and for PH_3 (g) + $TiCl_4$ (g) ⟶ $PH_3,TiCl_4$ (cryst.) it is 27·7. Hydrogen sulphide forms similar complexes, $H_2S,AlCl_3$ (cryst.) and $H_2S,TiCl_4$ (cryst.), for which the corresponding values are 43·1 and 18 kg.-cals./g.-mol., respectively.

In attempting to arrive at the desired values from these obviously incomplete data, several points must be borne in mind. Some of the values given, being heats of forming the solid product, include an unknown heat of vaporisation of perhaps 10 kg.-cals./g.-mol. or more. Those for the formation of the N→O link include resonance energy (see above). Obviously, too, the apparent heat of forming a co-ordinate link between a given pair of atoms is greatly affected by the other atoms or groups in the molecule.

For these reasons, only a rough answer can be expected: but it seems, both from these data and from our qualitative observations on the stability of some of the complexes, that the apparent heat of forming a

* The bearing of this hypothesis on the structure for ozone is discussed later (p. 161).

† This is similar to the possibility considered by Bauer, Finlay, and Laubengayer (*loc. cit.*), and rejected in the case of dimethyl ether–boron trifluoride, that the donor and acceptor components are linked through an electrostatic polarisation of the former by the latter. In any classical electrostatic treatment, the so-called exchange forces are ignored; but if the degree of interaction were small, the difference between this and the quantum mechanical treatment would be small.

‡ It may be noted that the order of strength of the bonds, PO > SO > ClO, is also that of the differences of electronegativity of the elements for their normal valencies, *viz.*, 1·4, 1·0, 0·5; the H_a values given above are, in fact, all about 100 times these differences.

co-ordinate link from phosphorus or sulphur to an acceptor molecule is not greater than the heat of forming one from nitrogen or oxygen to the same molecule (cf. Davidson and Brown, *J. Amer. Chem. Soc.*, 1942, **64**, 316); and that the heat of forming a co-ordinate link from nitrogen to oxygen is very roughly the same as that for one to aluminium chloride. Hence, we conclude that the heat of forming the S→O or the P→O bond would probably be not greater than 40 and certainly not more than 70 kg.-cals./g.-mol.

Rough as these values are, there seems no real doubt that the PO and SO oxy-bonds are much stronger than they would be if they were co-ordinate links: indeed, they are stronger than any such links yet investigated. Hence, their lengths, strengths, and electric dipole moments all lead to the conclusion that they are not this type of link. For the PS, PSe, SeO, and TeO oxy-bonds the case is not so complete; but the available evidence strongly favours this conclusion for them too.

The Description of the Oxy-Bonds.—Having decided with some certainty what the oxy-bonds are not, we must now consider what they are.

It has been suggested that they are double bonds and that *d* orbitals of the central atom are involved (Pauling and Brockway, *J. Amer. Chem. Soc.*, 1937, **59**, 13; Hampson and Stosick, *ibid.*, 1938, **60**, 1814; Brockway and Beach, *ibid.*, p. 1836; Beach and Stevenson, *J. Chem. Physics*, 1938, **6**, 75). Their heats of formation are of the right order: on p. 156 a value of 103 kg.-cals. was given for that of the SO bond, and others of 127·5 and 138 for that of the PO bonds. These are 1·42 and 1·76—1·91 times the respective calculated heats of forming the single S–O (72·4 kg.-cals.) and P–O (72·1) links. The former value may also be compared with that of the SO ($^3\Sigma^-$) molecule, which is probably 92·3 kg.-cals. (see Herzberg, "Molecular Spectra and Molecular Structure," I, New York, 1939, p. 493), wherein the link, like that in the O_2 ($^3\Sigma_g^-$) molecule, should be similar in strength to a double bond. Furthermore, the heat of formation per SO bond in sulphur dioxide is 127·7 kg.-cals., and in sulphur trioxide it is 112·5 kg.-cals. These compounds may, therefore, also be consistently formulated with double bonds.

This hypothesis would lead us to expect that the oxy-bonds should be quite definite entities, as in fact they seem to be. We have already remarked how near to 1·44 A. are the SO bond lengths in Table I; that of the similar bond in the SO ($^3\Sigma^-$) molecule is 1·49 A. (value estimated for double bond, 1·49 A.). The PO and PS oxy-bonds show rather more variation in length, but are still fairly constant.

Furthermore, the formation of an oxy-bond often has no effect upon the length of the other bonds (Brockway and Beach, *loc. cit.*; see also phosphorous and phosphoric oxide in Table I) though in thionyl chloride (Palmer, *ibid.*, 1938, **60**, 2360), dimethylsulphone, and the trithionate ion the other bonds are appreciably lengthened (see p. 148). This is much what would be expected, since an increase in covalency brings about a slight increase in bond length in other cases, *e.g.*, the octahedral covalent radii are about 3% longer than the tetrahedral ones (Pauling, *op. cit.*, p. 184); and l_{PF} in phosphorus pentafluoride is 1·57 A. against 1·52 A. in the trifluoride, likewise l_{PCl} in the pentachloride is 2·04—2·11 A. against 2·00 A. in the trichloride.

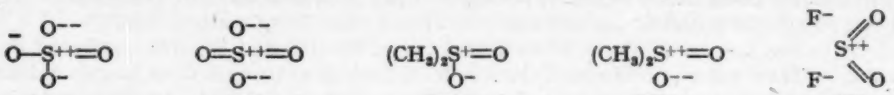
The dipole moments of the bonds are also relatively constant. Values calculated for the SO bond all lie between 2·2 (see Coop and Sutton, *Trans. Faraday Soc.*, 1939, **35**, 505) and 2·9, except in sulphur dioxide, wherein it is only 1·6; those for the PO bond between 2·7 and 3·5; those for the PS bond between 2·4 and 3·1.

From the discussion of bond lengths, it follows that the shortness of the oxy-bonds, compared with the lengths predicted for normal double bonds in the lower valency states, is abnormal and needs explanation. Palmer (*J. Amer. Chem. Soc.*, 1938, **60**, 2360) suggested that triple-bonded structures of the type $\overset{-}{X}\equiv\overset{+}{O}$ make a considerable contribution. If this were so, however, the dipole moments of the bonds should be very small, or even have the positive pole on the oxygen; and this is not the case (Lister and Sutton, *Trans. Faraday Soc.*, 1939, **35**, 495).* Such effect of the polar triple bond could only be compensated by an equal contribution from the single, co-ordinate linked structure $\overset{+}{X}—\overset{-}{O}$; but since this individual structure would, according to the previous evidence, be much less stable than either the double- or the triple-bonded ones, and since furthermore there is no automatic relation between the contribution of this and of the triple-bonded one as there is for example in carbon dioxide, where the contributory structures may be written $O{=}C{=}O$, $\overset{+}{O}\equiv C—\overset{-}{O}$, $\overset{-}{O}—C\equiv\overset{+}{O}$, there is no apparent reason why this structure should make more than a minor contribution (cf. Pauling, *op. cit.*, Chap. I). In turn, therefore, it is improbable that the triple-bonded structure can be important.

Pauling has attempted to account for the similar abnormalities in the sulphate ion (*op. cit.*, p. 241) by supposing that there is a contraction of radius brought about by the formal charges on the sulphur atom in such contributory structures as (I) and (II), which affects the length of the double bonds therein. This explanation implies that the resultant bond length is determined mainly by the "stiffest" component, *i.e.*, the double bond; but this principle seems to be one of some generality and may therefore be granted (cf. Pauling, *op. cit.*, p. 175). Applying it to the thionyl, sulphuryl, and phosphoryl compounds, we should expect the SO bonds to be of markedly different length in dimethylsulphone and sulphoxide, since ionic structures of the type (III) or (IV), which are at least conceivable in the former, are not in the latter. The actual difference is, however, small; for l_{SO} in the former is 1·44 (Table I) and in the latter 1·46 A. We should also expect

* For further data relating to the SO bond see Hampson, Farmer, and Sutton, *Proc. Roy. Soc.*, 1933, **143**, 147. This is shown for the PO link by the moments of triphenylphosphine oxide (4·28) and of *pp'p''*-trichlorotriphenylphosphine oxide (0·65) (see experimental section).

a marked difference for dimethylsulphone and sulphuryl fluoride or chloride, since in the latter it is possible that the positive charge on the sulphur atom would be increased by the partial ionic character of the sulphur–halogen bonds, *e.g.*, (V), whereas in dimethylsulphone any ionic charge from the carbon–sulphur bonds would



(I). (II.) (III.) (IV.) (V.)

be negative; yet in both the fluoride and the chloride the length is 1·43 A. Still another objection is that such a change in radius should affect *all* the bonds springing from the central atom; whereas actually the C–S bond in dimethylsulphone, like the S–S bonds in the trithionate ion $[SO_3–S–SO_3]^{--}$ (Pauling, *op. cit.*, p. 241), is rather *longer* than a normal single bond. Shortening by this sort of polar effect seems, therefore, to be only of minor importance.

The best course is to abandon for the present these attempts to find a detailed, mechanistic explanation of the phenomenon, and to relate it to a general principle which is gaining recognition, *viz.*, that there is a connection between the length and strength of a bond, inasmuch as abnormally strong bonds tend to be abnormally short, and weak ones long (cf. Hampson and Stosick, *loc. cit.*; Lister and Sutton, *loc. cit.*; Sutton, *Ann. Reports*, 1940, **37**, 78; Schomaker and Stevenson, *loc. cit.*, 1941). The system for calculating single-bond lengths from covalent radii and the Pauling electronegativity co-ordinates proposed by Schomaker and Stevenson is an attempt to state this principle precisely and quantitatively for a special case, since the co-ordinates in question are derived from abnormalities of bond energies (Pauling, *op. cit.*, Chap. II).

Although, as we have seen, the bond length in phosphorus pentafluoride is greater than it is in the trifluoride (1·57 and 1·52 A., respectively), it still is less than the sum of the single covalent radii (1·80 A., using the revised fluorine value; see Schomaker and Stevenson, *loc. cit.*); and in sulphur hexafluoride it is 1·57 instead of 1·76 A. Similarly, we should expect that double bonds to oxygen X=O, which almost certainly have heats of formation greater than the mean of X=X and O=O, would have lengths less than those calculated from normal radii. The values of these radii are by no means certain (see tables in Pauling and Huggins, *Z. Krist.*, 1934, *A*, **87**, 205; Pauling and Brockway, *J. Amer. Chem. Soc.*, 1937, **59**, 1223; Pauling, *op. cit.*, p. 164): that for O= has been variously given as 0·59, 0·55, and 0·57 A., while from the oxygen molecule ($^3\Sigma_g^-$), with a bond very similar to a double one, it is 0·604 A. Those used in Table I are from Pauling's list; and they probably allow for some contraction, such as would occur in a bond of moderate strength, as did the older single-bond covalent radii. Taking the normal O= radius as 0·60, and those for S=, Se=, P=, Cl=, and C= as 0·94, 1·07, 1·00, 0·89, and 0·665 A. (Pauling, *loc. cit.*), we derive the calculated double bond lengths: S=O, 1·54; Se=O, 1·67; P=O, 1·60, P=S, 1·94; Cl=O, 1·49; and C=O, 1·27 A. If now the Schomaker and Stevenson correction $[-\ 0{\cdot}09(x_A - x_B)]$ be applied, Pauling's electronegativities being used for the elements in their lower valency states, these become 1·43, 1·57, 1·46, 1·91, 1·49, and 1·18 A., the observed values being 1·44, 1·61 (in selenium dioxide), 1·39—1·55, 1·85—1·94, 1·44—1·48, and 1·21 A. Although this procedure is very arbitrary, the rough consistency of the results indicates that the underlying principle is at least qualitatively correct.

Two arguments have been advanced against the double-bond formulations; and they must be answered. One (p. 147) is that the so-called double bonds do not all add on water (Werner, *loc. cit.*). The other may be stated as follows. Elements in the second short period, unlike those in the first, show little tendency in general to form multiple links in their lower-valent states (Pauling, *op. cit.*, p. 232); *e.g.*, the S_8 and P_4 molecules have been shown to contain single bonds only, and $S_8 \longrightarrow 4S_2\ (^3\Sigma^-) - 96{\cdot}8$ kg.-cals., $P_4 \longrightarrow 2P_2 - 28{\cdot}2$ kg.-cals. (Rossini and Bichowsky, *op. cit.*); phosphorus trioxide exists as P_4O_6 with a single-bonded cage structure (Maxwell, Hendricks, and Deming, *J. Chem. Physics*, 1937, **5**, 626; Hampson and Stosick, *loc. cit.*) and not as O=P—O—P=O; silicon dioxide exists as a single-bonded, three dimensional polymer $(SiO_2)_n$ instead of O=Si=O. Therefore, it is argued, the oxy-bonds are unlikely to be multiple. These two arguments prove to be related.

Addition of water, $XO + H_2O \longrightarrow X\langle^{OH}_{OH}$, or polymerisation, $nXO \longrightarrow (—O—X—)_n$, will occur, roughly speaking,* only if $2H_a(X—O) > H_a(XO)$, *i.e.*, $H_a(XO)/H_a(X—O) < 2$. The oxides of second short period elements readily add on water or polymerise in such a way as to produce that number of single bonds which is equal to the lower or contra-valency, but not more. This shows that the above condition is satisfied for double bonds relative to single ones which in number do not exceed this limit. Werner's argument assumes, however, that it is also satisfied when the number of single bonds is increased further; but this is not a necessary consequence. Sidgwick and Bowen (*Ann. Reports*, 1931, **28**, 387; cf. Sidgwick, "The Covalent Link in Chemistry," Cornell, 1933, p. 120) have shown that the ratio of the heats of forming a double bond to that for the corresponding single one is sometimes less than 2 and sometimes more; *e.g.*, it is less than 2 for the

* In this statement, changes of entropy are ignored. So also are changes in intermolecular energies and heats of ionisation. The last should encourage addition of water; so the critical value of the ratio for this process may actually be more than 2. The effect of changes of intermolecular energy can be minimised by taking reactants and products in the same phase.

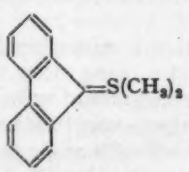
homoatomic links formed by carbon and all the elements after the first short period for which there are data; and for those formed by nitrogen and oxygen it is more, as it is also for carbon–oxygen links (2·0—2·2). This suggests that for elements of variable valency the ratio may possibly be less than 2 if the number of single bonds formed does not exceed the lower valency, but greater than 2 relative to any extra single bonds; and therefore that further hydration does not occur because of the relative weakness of the latter. This view, that single bonds formed in going from the lower to the higher covalency are weaker than the first type, is supported by the non-existence of any covalent higher halides of sulphur except the fluoride, and by the observed differences between the heats of forming the three P–Cl bonds in phosphorus trichloride (62·8 kg.-cals. each) and the two extra ones in the pentachloride (39·4 each). The difference in strength may be due to steric effects, to the extra bonds involving *d* orbitals of the central atom—though the oxy-bonds, if double, must do this too—or to both causes. It is much less marked in the heavier elements. For example, whereas triphenyl-phosphine and -arsine oxides form hydrates which are polar, yet triphenylstibine oxide forms a five-covalent dihydroxide $SbPh_3(OH)_2$ (Jensen, *Z. anorg. Chem.*, **1943**, **250**, 268). Telluric acid hydrates up to $Te(OH)_6$, $Te(OCH_3)_6$ is known, and $TeCl_4$ is quite stable. Periodic acid hydrates to $IO_2(OH)_3$ and to $IO(OH)_5$; and ICl_3 is comparatively stable. These facts suggest that the phenomenon may be steric in origin; but the detailed structure of phosphorus pentachloride (Pauling, *op. cit.*, p. 109) indicates that there is a difference of the bonding orbitals for the two bonds along the axis from the three in the belt of the trigonal pyramid (cf. Wells, *Z. Krist.*, **1938**, **99**, **367**, on the trimethylstibine dihalides).

In the other argument, it is supposed that the reason for the polymerisation is the absolute weakness of the multiple bonds. We have shown, however, that this is only proof of a relative weakness. The P≡P link may be weak (H_a = 42·1 kg.-cals., Bichowsky and Rossini, *op. cit.*; but Herzberg, *op. cit.*, gives 116); but the S=S ($^3\Sigma_g^-$) bond is quite strong (103·4, Rossini and Bichowsky; Herzberg gives 83) and the Si=O bond is still more so [162 in SiO_2(g), Bichowsky and Rossini; 170 in SiO, Herzberg]. Hence, we should not expect multiple bonds to oxygen, formed in attaining the higher valency, to be weak on an absolute scale; nor, as we have seen above, need they be weak relatively.

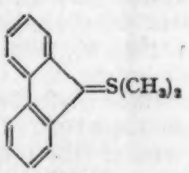
The behaviour of sulphur dioxide and trioxide illustrates the relation between polymerisation and addition of water developed above. The former does not polymerise; but the latter does (the Trouton constants are 23·1 and 32·4 cals./degree respectively)—in the α- or γ-form to $O_2S\langle^{O—SO_2}_{O—SO_2}\rangle O$ (Smits and Moerman, *Rec. Trav. chim.*, **1937**, **56**, 169) and in the β-form to $(—O—SO_2—)_n$ (Gerding and Moerman, *Z. physikal. Chem.*, 1937, *B*, **35**, 216). This indicates that $H_a(S=O)/H_a(S—O)$ is greater than 2 for the former and less than 2 for the latter; *i.e.*, since $H_a(S=O)$ is 127·7 and 112·5 kg.-cals., respectively (p. 157), that the estimated value on p. 157 for $H_a(S—O)$ is too large and that it really is between 63·75 and 56·25 kg.-cals. Correspondingly, sulphur dioxide should not add water to form hydroxyl groups so readily as does the trioxide. This is so (see Ley and König, *ibid.*, **1938**, *B*, **41**, 365); but, no doubt owing to the rather small margin, even the latter does not do so completely—100% sulphuric acid gives off the trioxide.

From this discussion we see that a reasonably consistent explanation of the physical characteristics and chemical properties of the oxy-compounds of phosphorus, sulphur, selenium, and chlorine can be given on the assumption that the oxy-bonds are double. It is still possible, of course, that the co-ordinate link structures make some contributions; but unless the values for their energies previously estimated (p. 157) are much too small, these contributions are minor. If we assume that they are the sole cause of the bond dipole moments, they are equal to x of the table on p. 155, *i.e.*, 0·35—0·44; but it is very probable that the double covalent bonds themselves are polar (Mulliken's " homopolar dipole," *J. Chem. Physics*, **1935**, **3**, 573; cf. Coulson, *Trans. Faraday Soc.*, **1942**, **38**, 433), and hence that the contributions are much smaller. These oxy-bonds are, therefore, best described as double. For those formed by arsenic and antimony no such definite opinion can yet be expressed, owing to the lack of data.

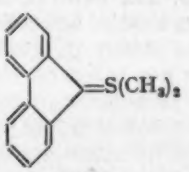
The Sulphur–Carbon Link in Dimethylsulphonium-9-fluorenylidide.—From the foregoing arguments, it might be expected that this bond would be double. It can be so formulated in an otherwise reasonable structure (VI). The dipole-moment data in Table II show, however, that this is not the case. We must, therefore, seek the reason for this apparent anomaly. The theory of the stabilisation of molecules by resonance (Pauling, *op. cit.*, Chap. IV) supplies it. If the sulphur–carbon link were double, the only resonance stabilisation possible would be that provided by the alternative Kekulé structures for the benzene rings (VII, VIII), *i.e.*, there is none peculiar to the system as a whole. If, however, the link is single, there are many possi-



(VI.)



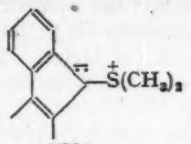
(VII.)



(VIII.)

bilities of new component structures, for the unshared electrons which would be left on the carbon skeleton could be on any of the 13 atoms composing it. A few of these are shown in (IX)—(XII). All would be highly

polar, because the donor atom carrying the positive charge and the unshared pair of electrons carrying the negative one are widely separated.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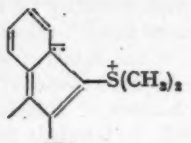
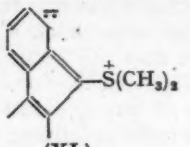
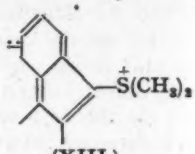

(X.)


(XI.)


(XIII.)

Hence, the single-bonded would be stabilised relative to the double-bonded structure; and it would be very important, or possibly predominant, even if the >S=C< link were as strong as the >S=O link. If the S=C link were very weak, the single-bonded structure would still be possible: the resonance stabilisation then would probably be the only reason why the complex hangs together.

The substance loses methyl sulphide very readily. The other product is probably a large condensed hydrocarbon which is also considerably stabilised by resonance. Unless there is a large difference between the resonance energies in reactant and product, this instability indicates that the two sulphur–carbon links are weak relative to one double carbon–carbon bond, and hence that the latter of the two possibilities considered above is correct.

The Phosphorus–Nitrogen Link in the Phosphinimines.—The nature of this bond in triphenylphosphine-phenylimine, $PPh_3{:}NPh$, is not clear from the present data. The numerical difference of the moments (in solution) of triphenylphosphine and its phenylimine is 3·01; but, since the molecule lacks an axis of symmetry, this is less than the vector change. A rough estimate of the moment of the phosphorus–nitrogen bond, got by assuming $\mu_{Ph-N} = 1{\cdot}5$, $P\widehat{-N}-Ph = 125°$, and making corrections for the solvent effects and resonance moments, is 4·2. If, however, we try also to allow for the mutual induction between moments, following Groves and Sugden (J., 1937, 1992), the moment obtained is 3·0. So μ_{PN} is probably 3—4.

The bond may therefore be more nearly a co-ordinate link than is either the P–O or the P–S bond. It appears also to be rather weaker, since treatment of the phenylimine with mineral acids readily gives the phosphine oxide, while boiling with carbon disulphide gives the sulphide (Staudinger and Meyer, *Helv. Chim. Acta*, 1919, **2**, 664). These facts could be explained if the >P=N— bond were for some reason less stable than the others. There is no obvious reason why it should be—the difference of the Pauling electronegativities for phosphorus and nitrogen is almost the same as that for sulphur and oxygen—but in this particular substance the possibilities of resonance complicate the discussion of its structure or reactions, and data for simpler phosphinimines are desirable.

Brockway and Beach (*J. Amer. Chem. Soc.*, 1943, **65**, 1551) found the phosphorus–nitrogen distance in the six-membered ring of the polymer $(PNCl_2)_3$ to be 1·65 ± 0·04 A., and concluded from this that the bonds are, like those in benzene, intermediate in order between single and double, therefore that the ring is of benzenoid type, and hence that the phosphorus is quinquevalent. This conclusion is consistent with the new system of calculating bond lengths. If the following covalent radii for phosphorus and nitrogen be assumed, *viz.*, P—, 1·10 (Pauling); N—, 0·74 (Schomaker and Stevenson); P=, 1·00 (Pauling); N=, 0·65 A. (*i.e.*, 0·05 A. greater than the O= radius from O_2), and the Schomaker and Stevenson correction is applied as before, l_{P-N} is calculated as 1·76, and $l_{P=N}$ as 1·57 A. From these values, the length of the benzenoid P–N bond should be 1·62 A.

Stereochemical Considerations.—The non-planar configurations of the sulphoxides and related compounds, like the bent one of sulphur dioxide, are no longer regarded as decisive evidence against the sulphur–oxygen bond being double. It is realised that the stereochemistry of sulphur with a decet of electrons in the valency group would probably be based not on the regular tetrahedron but on the trigonal bipyramid, like that of quinquecovalent phosphorus (Palmer, *J. Amer. Chem. Soc.*, 1938, **60**, 2360; Lister and Sutton, *Trans. Faraday Soc.*, 1939, **65**, 495; Stevenson and Schomaker, *J. Amer. Chem. Soc.*, 1940, **62**, 1267; Kimball, *J. Chem. Physics*, 1940, **8**, 188).

The stereochemistry of sexacovalent sulphur should be based on the regular octahedron, as in the hexafluoride (Braune and Knoke, *Z. physikal. Chem.*, 1933, *B*, **23**, 297; Brockway and Pauling, *Proc. Nat. Acad. Sci.*, 1933, **19**, 860). Hence, the trioxide, if all three bonds were double, should be planar, as in fact it is (Smits, Moerman, and Pathuis, *Z. physikal. Chem.*, 1937, *B*, **35**, 60; Palmer, *loc. cit.*): sulphuryl chloride and the sulphones should, however, be tetrahedral (Kimball, *loc. cit.*).

Brockway and Beach (*J. Amer. Chem. Soc.*, 1938, **60**, 1836) showed that the stereochemistry of the phosphoryl halides is not based on the regular tetrahedron, the X—P—X angles being close to 106° instead of 109·5°. It may be noted that the sum of the three angles between three neighbouring bonds in a trigonal bipyramidal arrangement is 300°; the mean is therefore 100°. Our data for the moments of triphenylphosphine oxide and its *pp'p''*-trichloro-derivative give a value of 112° ± 5° for the Ph—P—Ph angle, indicating enlargement by the steric repulsion of the phenyl groups. No definite value for the Ph—P—Ph angle in triphenylphosphine can be got from our data for this and its trichloro-derivative, because the direction of the latter moment relative to the first is not known: hence there are two possible answers, 117° ± 5° and 101° ± 5°.

The Structure of Ozone.—No completely satisfactory explanation of the properties of ozone has yet been

given. Its electric dipole moment is only 0·49 (Lewis and Smyth, *J. Amer. Chem. Soc.*, 1939, **61**, 3063); the bonded O–O distance is 1·26 ± 0·02 A. (Shand and Spurr, *ibid.*, 1943, **65**, 179), *i.e.*, it is intermediate between the single-bond length, 1·46 A. (Giguère and Schomaker, *ibid.*, p. 2025) and that in the oxygen molecule, 1·20 A. (see above); the angle $\widehat{O—O—O}$ is 127° ± 3°; and the heat of forming each bond from the atoms is only 71·4 kg.-cals. (data from Bichowsky and Rossini, *op. cit.*). Shand and Spurr sought to explain the small moment by supposing that there is hybridisation not only between two structures of the type $O{=}O^{+}\!-\!\bar{O}$, but also with two of the type $O^{+}{-}O{-}O^{-}$ which cancel each other's polarity. Calculating the contribution of the latter from the observed O–O bond distance, and hence calculating the electric moment, they find it still to be 1·62; and if they had taken the oxygen double bond radius as 0·60 instead of 0·55 A., they would have got a still bigger value. So the small one observed remains puzzling.

On p. 155 it was shown that the moments of complexes are not as large as they would be if the electrons forming the co-ordinate link were symmetrically shared. The actual bond may, therefore, be formally described as a hybrid between an unbound state A B and a symmetrical or perfect co-ordinate link $\overset{+}{A}\!-\!\overset{-}{B}$. The former obviously has a high energy content because the unbound atoms repel each other. The latter is stabilised relative to the former by having a covalent link and an ion-pair bond too, but it is destabilised by the difference between the energy required for the ionisation of A and that given out by the corresponding addition of an electron to B. An intermediate state may therefore be more stable than either extreme: the greater the energy content of the extreme polar state, the nearer would the actual one be to the unbound extreme; and consequently the less its polarity, and the less its stability relative to the dissociated state A plus B.

The low moment and low heat of formation of ozone are therefore related. Ozone and the nitro-group make an interesting contrast: the moment of the former being 0·49, and of the latter *ca.* 2·5 ($\mu_{CH_3\cdot NO_2} = 3{\cdot}1$; $\mu_{CH_3N} = 0{\cdot}6$) and the heat of the reaction $O_2 + O \longrightarrow O_3$ being only 14·6 kg.-cals. against *ca.* 68 for $—N{=}O + O \longrightarrow —NO_2$. It seems probable that the structure may be best described as a hybrid between two component structures of the type $O{=}O^{+}\!-\!O^{-}$ and two of the type $O{=}O$ O, the latter predominating. The possible components $O^{+}{-}O{-}O^{-}$ are likely to be of an even higher energy content, and so to be unimportant. On the principle that the resultant bond length is disproportionately near to that with the greater stretching force constant (cf. p. 157), we should expect the O–O distance to be greater than, but quite close to, that in the oxygen molecule which also is paramagnetic, and the valency angle to be greater than 120°. In this way, therefore, the salient characteristics of the molecule can be explained.

The Existence of the Halogen Oxy-acids.—Although the oxy-acids of the heavier halogens have long been known, fluorine has not yet been shown definitely to form any (*Ann. Reports*, 1936, **33**, 147). From the present discussion we may conclude that it probably cannot, save possibly hypofluorous acid.

Generalising from what we have learnt about oxy-bonds, we may suggest that the higher oxy-acids of chlorine, bromine, and iodine exist only because these elements are able to utilise *d* orbitals to form double bonds to oxygen. Nitrogen forms nitric acid, with a co-ordinate link to oxygen; but it is much more easily reduced than is phosphoric acid. Oxygen forms no oxy-acid in this sense, though sulphur forms many. Covalent fluorine would not be expected to form co-ordinate links more readily than covalent nitrogen or oxygen, but less so, for it has a greater nuclear charge. Therefore we should not expect it to form any oxy-acid other than hypofluorous acid in which it is univalent.

Conclusions.—Two general conclusions emerge. One is that co-ordinate links occur much less commonly than they were once thought to do. To emphasise this, we may recall that bond-length measurements provide evidence for the bonds in several types of complex formed by transition elements being partly or wholly double in character (Pauling, *op. cit.*, pp. 250—258), instead of the single, co-ordinate links they were formerly thought to be. They do occur; but on the whole they seem to be relatively weak. Their occurrence is sometimes favoured by the increase of resonance energy of a system into which they bring possibilities of more component structures, as in the nitro-group, ozone, and in dimethylsulphonium-9-fluorenylidide.

The factors which determine their strength seem fairly obvious, although they have not been quantitatively sorted out in any particular case: they are (1) the strength of a covalent link between the two elements in their charged states, which probably will be much the same as that of a pure covalency one between the uncharged ones, (2) the energy of ionisation and the electron affinity of the donor and acceptor atoms, respectively, (3) the energy of the ionic link, (4) the repulsion energy of the two parts of the complex when brought to within bond-forming distance, excluding the repulsion terms between the actual donor and acceptor atoms which are included in (1) and (3), but including such terms as repulsion energy between attached groups, and distortion energy.

The sharing of the bonding electrons between the donor and the acceptor atoms is found not to be symmetrical: they are always nearer the former. Polarity and strength should increase or decrease together.

The second general conclusion is that the properties of the oxy-bonds in the higher oxides and oxy-acids of phosphorus, sulphur, selenium, and chlorine can be very well explained on the hypothesis that they are double. Certain minor premises involved in this explanation, adopted rather as empirical generalisations, themselves require to be elucidated in terms of more fundamental concepts, *e.g.*, the generalisation that abnormally strong bonds are short and weak ones long, and the limited generalisation that the single bonds

formed in reaching the lower covalency are stronger than the extra ones formed in reaching the higher covalency although double bonds are not similarly affected. But the general correctness of the hypothesis now seems well established; and its recognition leads to the solution of a number of problems of long standing.

The authors wish to thank Prof. N. V. Sidgwick, F.R.S., for many searching criticisms, and Imperial Chemical Industries Ltd. for a grant towards the cost of the investigation.

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39. *Quantitative Determination of Methylglyoxal, and the Mechanism of its Reaction with Hypoiodite Solution.*

By SHO-CHOW WOO and SZE-TSENG CHANG.

It has been shown that the reaction established by Fischler and Boettner, *i.e.*,

$$CH_3{\cdot}CO{\cdot}CHO + 4I_2 + 7NaOH = CHI_3 + (CO_2Na)_2 + 5NaI + 5H_2O \quad . \quad . \quad . \quad . \quad (1)$$

cannot be used as a quantitative method for determining methylglyoxal. The degree of completeness of this reaction varies greatly with the experimental conditions, never exceeding 94%. Excess of iodine and sodium hydroxide have been shown to convert methylglyoxal into pyruvate and oxalate, and an accurate quantitative method has been based on this reaction, the iodine consumed and the oxalate produced being determined.

The mechanism of the total reaction is discussed.

WE have examined several methods for the determination of methylglyoxal. Friedemann's method (*J. Biol. Chem.*, 1927, **73**, 331) gave consistent results, but that of Fischler and Boettner (*Z. anal. Chem.*, 1928, **74**, 28), though sometimes consistent in itself, gave lower results. Since in neither case was there an independent check by a trustworthy process, the absolute accuracy of these two methods is unknown. Takahashi (*J. Biochem. Japan*, 1933, **17**, 299) found that the latter method gave results 6% lower than the former and nearer to those obtained by Neuberg and Kobel's method (*Biochem. Z.*, 1928, **203**, 463), but nevertheless concluded that these three methods were the best available.

Since anhydrous methylglyoxal is difficult to prepare and very hygroscopic, the methods could not be checked against accurately weighed quantities, so another procedure had to be devised. Fortunately, by the methods of Riley, Morley, and Friend (J., 1932, 1875) and Riley and Gray (*Org. Synth.*, 1935, **15**, 67), glyoxals may be prepared conveniently in pure condition, and by testing the methods on weighed quantities of pure phenylglyoxal monohydrate, one of us (S.-C. W.), together with (Miss) Wang Chêng-I, proved the accuracy of Friedemann's method to within an error of 1%.* Hence, the concentration of a methylglyoxal solution so determined could be used as a standard for examining the Fischler–Boettner method. This involves the use of an alkaline hypoiodite, and although this reaction has been much used for the determination of organic compounds, its dependence upon experimental conditions and its mechanism have only recently been thoroughly studied. Hatcher and Mueller (*Trans. Roy. Soc. Canada*, 1929, III, **23**, 35) and Hatcher and Horwood (*Canadian J. Res.*, 1934, **11**, 378) found that even for acetone the extent to which reaction proceeds is greatly influenced by the quantity of alkali used and by the order of mixing of the reagents. It is now generally accepted (see, *e.g.*, Fuson and Bull, *Chem. Rev.*, 1934, **15**, 275) that the rate of this reaction is chiefly controlled by the rate of enolisation of acetone, which, in turn, depends on the concentration of the alkali. It was thought that the reactions involved in the Fischler–Boettner method might show similar characteristics. Consequently, a systematic study of this method under various conditions was undertaken in order to elucidate its mechanism and that of hypoiodite in general, and to find an accurate method for the determination of methylglyoxal.

EXPERIMENTAL.

The methylglyoxal used was prepared by the method of Riley, Morley, and Friend (*loc. cit.*), the higher-boiling portion being further purified by vacuum distillation. The sodium hydroxide, iodine, iodate-free potassium iodide, sodium thiosulphate, potassium permanganate, and hydrochloric acid were of the highest grade of purity available, and their solutions were standardised as usual, results agreeing to within 0·2%. These were checked about every 10 days.

When methylglyoxal is mixed with an excess of iodine and sodium hydroxide solutions, iodoform and oxalate are produced [see (1), above], as proved by Fischler and Boettner. Their procedure was as follows: A solution of methylglyoxal was mixed with a measured excess (1—1·5 times the theoretical quantity) of N/10-iodine solution, the mixture made alkaline with 6—10 times the theoretical volume of N-sodium hydroxide, and, after ½ hour, acidified with hydrochloric acid, the liberated iodine being titrated with N/10-sodium thiosulphate. For the determination of iodoform and oxalate, a duplicate portion was treated with iodine and alkali exactly as above, and after ½ hour the iodoform was filtered off, washed, dried, and weighed, the oxalate in the filtrate being determined as calcium salt (monohydrated) by acidification with acetic acid and addition of calcium chloride.

Our preliminary experiments were done (*a*) by the above procedure; (*b*) by using hydrochloric acid, followed by calcium chloride and ammonia, as usual, to precipitate the oxalate; (*c*) by simplifying the procedure to make the three determinations in one solution. All three methods gave essentially the same results, so our final procedure was as follows: After the mixture of methylglyoxal, iodine, and sodium hydroxide had been kept for ½ hour, it was acidified with hydrochloric acid, the unconsumed iodine titrated with thiosulphate, and the iodoform filtered off on a sintered glass filter, dried in a vacuum desiccator, and weighed; to the filtrate, excess of calcium chloride solution was added, and calcium oxalate precipitated at 70—80° as usual, filtered off, dissolved in sulphuric acid and titrated with standard potassium permanganate.

* These results will be reported later, together with other methods for determination of phenylglyoxal.

From these results it was found that the concentration determined from the iodine consumed was lower than that determined by Friedemann's method, the yield of oxalate was somewhat lower than that calculated from the consumed iodine, and that of iodoform still lower. Moreover, the iodine consumed and the oxalate produced varied considerably with the experimental conditions. Consequently, a systematic investigation was made by wide variations in (1) the excess of sodium hydroxide, (2) the excess of iodine, (3) the concentration of alkali, and (4) the order and (5) the manner of mixing of reagents. Experiments were also carried out to determine the rate of reaction after the addition of alkali to the mixture of methylglyoxal and iodine.

Results and Discussion.

The results are summarised in the tables. In the main table, all the experiments were made by adding the alkali last. The three necessary determinations were then made.

. 10 *C.c. of* 0·1057 (*or* 0·0639)M-CH_3·CO·CHO + 40(*or* 80) *c.c.* of 0·3N-*iodine* + NaOH.

1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
							% of CH_3·CO·CHO converted into			
No.	CH_3·CO·CHO, millimols.	I_2 added, milliequivs.	NaOH, milli-equivs.	I_2, cons., milli-equivs.	$(CO_2Na)_2$, millimols.	CHI_3, millimols.	$(CO_2Na)_2$.	CH_3·CO·CO_2Na.	Total of 8 and 9.	CH_3·CO·CHO, millimols., calc.
1	1·057	12	7 (1N)	3·050	0·1542	—	14·59	85·9	100·5	1·063
	Series A : NaOH added gently down the sides of the flask, with shaking after each addition, and final dilution to 174 c.c.*									
2*a*	1·057	12	14 (1N)	5·537	0·5582	0·523	52·81	50·7	103·5	1·094
2*b*	1·057	12	14 (1N)	5·532	0·5683	0·526	53·77	46·6	100·4	1·061
2*c*	1·057	12	14 (1N)	5·262	—	—	—	—	—	—
3*a*	1·057	12	35 (1N)	7·301	0·8560	—	80·98	21·4	102·4	1·083
3*b*	1·057	12	35 (1N)	7·973	0·9761	—	92·34	7·8	100·1	1·058
3*c*	1·057	12	35 (1N)	7·331	0·8538	—	80·79	23·7	104·5	1·104
4*a*	1·057	12	84 (1N)	7·965	0·9726	0·888	92·02	8·7	100·7	1·065
4*b*	1·057	12	84 (1N)	7·959	0·9748	0·881	92·22	7·6	99·8	1·055
5*a*	1·057	24	14 (1N)	3·711	0·2863	0·233	27·09	67·2	94·3	0·997
5*b*	1·057	24	14 (1N)	3·797	0·2855	0·253	27·01	71·6	98·6	1·042
	Series B : NaOH added from a burette at normal rate.									
1	1·057	12	3 (1N)	1·251	—	—	—	—	—	—
2	1·057	12	5 (1N)	2·100	—	—	—	—	—	—
3	1·057	12	14 (1N)	4·458	(0·3907)	—	(37·0)	—	—	—
4	1·057	12	35 (1N)	6·744	(0·7716)	—	(73·0)	—	—	—
5	1·057	12	84 (1N)	6·588	(0·7457)	—	(70·6)	—	—	—
6	1·057	12	35 (2N)	7·837	(0·9539)	—	(90·3)	—	—	—
7	1·057	12	35 (4N)	7·927	(0·9689)	—	(91·7)	—	—	—
8*a*	0·639	12	14 (1N)	3·928	0·4433	—	69·37	29·89	99·26	0·634
8*b*	0·639	12	14 (1N)	3·916	0·4409	—	69·00	30·44	99·44	0·635
Series C : The quantity of N-sodium hydroxide, diluted to 84 c.c., was added dropwise with constant stirring.										
1	1·057	12	7 (N/12)	3·249	(0·189)	—	(17·9)	—	—	—
2	1·057	12	14 (N/6)	4·917	0·467	—	44·18	55·86	100·04	1·057
3	1·057	12	35 (5N/12)	4·950	(0·473)	—	(44·8)	—	—	—
4	1·057	12	56 (2N/3)	4·920	(0·468)	—	(44·3)	—	—	—
5	1·057	12	84 (1N)	5·244	(0·522)	—	(49·4)	—	—	—

* Under these conditions (see p. 165) the reaction stopped very quickly after the addition of alkali, and hence the dilution here would not show any effect.

From equation (1), 1 mol. of methylglyoxal should consume 8 equivs. of iodine and yield 1 mol. each of iodoform and sodium oxalate, but from the tabulated results the following facts may be noticed. First, the amounts of all these three species involved varied greatly with the quantity and the manner of addition of the alkali, and to a lesser extent, with the quantity of iodine and the concentration of alkali. Under all conditions, too little iodine was consumed; the highest value (expt. 3*b*) corresponds to $7{\cdot}973 \times 100/8 \times 1{\cdot}057 = 94\%$ of the methylglyoxal present, agreeing with Takahashi's value for the ratio between the results of the Fischler–Boettner and the Friedemann method. Secondly, the oxalate produced was always less than one-eighth of the iodine consumed; hence, some of the iodine must have been consumed in side reactions. Thirdly, the iodoform produced was even lower than the oxalate; this may be explained partly by the greater experimental error in its determination and partly by its appreciable solubility, *i.e.*, 0·0106 g. per 100 g. of water at 25° (Seidell, " Solubilities, etc.," van Nostrand, 1919, p. 335).

The aldehyde group of methylglyoxal may be easily oxidised by hypoiodite, and Neuberg and Corr (*Biochem. Z.*, 1925, **166**, 442) have oxidised it with bromine to pyruvic acid, the reaction being accelerated by sodium acetate; hence some of the iodine may have been used for oxidation of methylglyoxal to pyruvate :

$$CH_3{\cdot}CO{\cdot}CHO + I_2 + 3NaOH = CH_3{\cdot}CO{\cdot}CO_2Na + 2NaI + 2H_2O \quad . \quad . \quad . \quad . \quad (2)$$

This would require that

$$\text{Total } I_2 \text{ consumed} = 8[(CO_2Na)_2] + 2[CH_3{\cdot}CO{\cdot}CO_2Na] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

also $CH_3{\cdot}CO{\cdot}CHO$ converted into $(CO_2Na)_2 = [(CO_2Na)_2] \times 100/1{\cdot}057\%$

and " " " $CH_3{\cdot}CO{\cdot}CO_2Na = \dfrac{\text{Total } I_2 \text{ consumed} - 8[(CO_2Na)_2]}{2 \times 1{\cdot}057} \times 100\%$. (4)

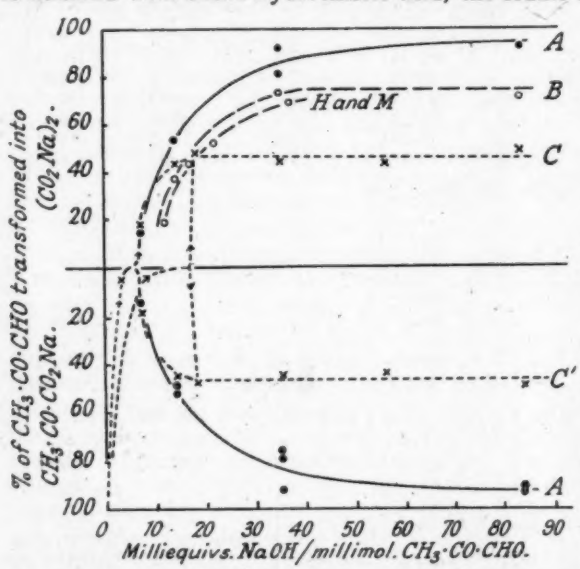
where iodine is expressed as milliequivs. and the salts in millimols. The percentages so calculated are listed in cols. 8 and 9 of the table (without parentheses). It will be seen from col. 10 that the total amount of methylglyoxal undergoing the reaction is 100±4%. This means that under any experimental conditions when iodine and alkali were in excess, all the methylglyoxal has been converted into pyruvate and/or oxalate. Although the 4% error seems large, it must be remembered that the experimental conditions varied over a very wide range; moreover, the pyruvate is obtained by difference in (3) and so is sensitive to experimental error.

Now if y is the number of millimols. of methylglyoxal and x is the fraction converted into oxalate, then $1 - x$ is the fraction converted into pyruvate, and (3) can be transformed into

$$\text{Total } I_2 \text{ consumed} = 8xy + 2y(1 - x) = 2y + 6xy = 2[CH_3{\cdot}CO{\cdot}CHO] + 6[(CO_2Na)_2] \quad . \quad . \quad (3a)$$

whence, if iodine and alkali are in excess, we can calculate the quantity of methylglyoxal from determinations of the iodine consumed and the oxalate produced. The results so obtained are given in col. 11, and although the error may be as high as 4%, many of the results (especially in series B and C) agree with the quantities, 1·057 or 0·639 millimols., determined by Friedemann's method. Furthermore, this method has the advantage of not being much affected by the experimental conditions. Hence, we suggest the following amplification of the details on p. 162.

The aqueous solution of methylglyoxal is mixed with about 12 equivs. of 0·1—0·3N-iodine, and then with 14—30 equivs. of N-sodium hydroxide, added from a burette and stirred. After a few minutes, the mixture is acidified with dilute hydrochloric acid, the iodine is titrated with sodium thiosulphate, and the iodoform filtered off. In the filtrate, oxalate is determined gravimetrically or volumetrically by standard procedure, and the weight of methylglyoxal calculated from equation (3*a*).



In order to determine whether pyruvate is formed at a low pH, and therefore before the oxalate, we made the following experiments.

(1) To find whether methylglyoxal and iodine react in absence of alkalis, 10 c.c. of 0·1057M-methylglyoxal were mixed with 40 c.c. of 0·3N-iodine and 124 c.c. of water; after ½ hour, the unconsumed iodine was titrated, but only 0·030 and 0·036 milliequiv. were used in two different experiments.

(2) To find whether there is any consumption of iodine before formation of iodoform in weakly alkaline solution, 30·5 c.c. of 0·1N-sodium hydroxide (barely sufficient for the formation of pyruvate only) were added dropwise with constant stirring to 10 c.c. of 0·1057M-methylglyoxal, 40 c.c. of 0·3N-iodine, and 94 c.c. of water. No iodoform was formed, but 1·99 and 2·03 milliequivs. of iodine were found to have been consumed on titration, respectively, immediately and after ½ hour. These correspond to 94 and 96% of conversion into pyruvate.

(3) To determine whether the first appearance of iodoform could be used as an indication of the completeness of the formation of pyruvate, 0·01N-sodium hydroxide was added dropwise with constant stirring to a mixture of methylglyoxal and iodine as in (2) with 40 c.c. of water till iodoform appeared; after ½ hour, the unconsumed iodine was titrated, and 5·20 milliequivs. found to have been consumed, corresponding to 48·7% conversion into oxalate.

From these experiments, it is clear that at low pH transformation into pyruvate predominates, but that higher pH favours formation of oxalate. We have the following consecutive and simultaneous reactions:

(i) $I_2 + 2NaOH = NaI + NaIO + H_2O$
(ii) $CH_3{\cdot}CO{\cdot}CHO + NaIO + NaOH = CH_3{\cdot}CO{\cdot}CO_2Na + NaI + H_2O$
(iii) $CH_3{\cdot}CO{\cdot}CO_2Na + 3I_2 + 4NaOH = CHI_3 + (CO_2Na)_2 + 3NaI + 3H_2O$

Reaction (i) is probably the most rapid, and although this would consume sodium hydroxide almost instantly if it were slowly added, there might be sufficient hydroxyl-ion concentration to facilitate reaction (ii). Only when this has been completed will reaction (iii) begin to take place with further addition of alkali, but the onset of this depends on the concentration and the manner of addition of the alkali as depicted by curves *C* and *C'* (see Fig.). However, in rapid addition of alkali, the local hydroxyl-ion concentration may suffice to start reactions (i), (ii), and (iii), simultaneously. This explains why the iodine consumed and the oxalate produced were so much influenced by the manner of addition of the alkali.

The formation of pyruvate as an intermediate step was also postulated by Fischler and Boettner, but its further oxidation requires such a high hydroxyl-ion concentration that, as shown by Hatcher and Mueller, it can never be complete when alkali is added to a mixture of pyruvic acid and iodine. From the iodine consumed, we have calculated by equation (4) the proportion of methylglyoxal transformed into oxalate; these

values are listed in the main table in parentheses and plotted in the figure. It will be seen that they vary with the manner of addition of alkali, approaching a different maximum which does not increase with further addition of alkali. These maximum values, though fluctuating somewhat, are different in each case. If the pyruvate is indeed the intermediate in the oxidation of methylglyoxal, these values are actually the proportion of pyruvate converted into oxalate. Consequently, the values of our series B experiments (see table) should agree roughly with those obtained by Hatcher and Mueller for pyruvic acid :

$$CH_3{\cdot}CO{\cdot}CO_2H + 3I_2 + 5NaOH = CHI_3 + (CO_2Na)_2 + 3NaI + 4H_2O \quad . \quad . \quad . \quad . \quad (1a)$$

The results of those authors, for 1 millimol. of methylglyoxal and 14 milliequivs. of iodine, were as follows (with a slight modification to allow for iodine and alkali used for oxidation of the aldehyde to the acid) :

NaOH, milliequivs.	12	17	22	27	32
% Conversion into $(CO_2Na)_2$	18·5	43·5	52·0	62·4	68·8

These values are also plotted in the figure. It will be seen that they agree well with our curve B, except for small differences which might arise from differences in manner of addition and in the quantities of iodine used for these two cases.

It might still be doubted whether the difference in oxalate production could not be partly due to an error arising from not stopping the reaction immediately after the addition of alkali. Preliminary experiments for the determination of reaction rate were thus made for the different manners of addition and different quantities of sodium hydroxide. It was found that, under our experimental conditions, the reaction practically stopped after 10 mins., no difference being detected after a further 50 mins.

Hatcher and his collaborators also found that for acetone and pyruvic acid the rate of the reaction producing iodoform is controlled by the enolisation of these compounds, which again depends on the pH value. Consequently, the completeness of the reaction depends upon the order of mixing of the reagents. Orders of addition being denoted by (I) $CH_3{\cdot}CO{\cdot}CO_2H$, NaOH, I_2; (II) $CH_3{\cdot}CO{\cdot}CO_2H$, I_2, NaOH; (III) I_2, NaOH, $CH_3{\cdot}CO{\cdot}CO_2H$, Hatcher and Mueller found that in (I), reaction approached almost to completion when the alkali exceeded 6 times the theoretical quantity; in (III) the reaction proceeded the least. Our results for methylglyoxal agree fairly well with those of series (II) in their work, but we have also made experiments upon this compound with the other two orders of mixing, the results of which are given below.

Order of mixing.	$CH_3{\cdot}CO{\cdot}CHO$, millimols.	H_2O, c.c.	N-NaOH, milliequivs.	I_2 added, milliequivs.	I_2 consumed, milliequivs.	$(CO_2Na)_2$, millimols.
$CH_3{\cdot}CO{\cdot}CHO$, NaOH, I_2	1·057	40	14	12	2·765	0·3368
I_2, NaOH, $CH_3{\cdot}CO{\cdot}CHO$	1·057	40	14	12	0·114	—

With the last order of mixing, the consumption of iodine was very small, the pH in the hypoiodite solution apparently being too low even for the formation of pyruvate. The other order of mixing would have resulted in a large production of oxalate were it not for the fact that methylglyoxal might have undergone a Cannizzaro reaction, affording lactate, before it could be oxidised to pyruvate; nevertheless, the methylglyoxal which had not undergone this reaction must have been almost completely converted into oxalate. (It is presumed that lactate is much more slowly oxidised than pyruvate.) Hence, although the iodine consumed and the oxalate produced were both too low, the latter corresponded to 97·4% of the total iodine consumed.

In another experiment, instead of sodium hydroxide, 14 milliequivs. of N-sodium acetate were added to a mixture of 10 c.c. of 0·1057M-methylglyoxal, 40 c.c. of 0·3N-iodine, and 40 c.c. of water; after ½ hour, only 0·099 milliequiv. of iodine had been consumed.

This work is being continued.

INSTITUTE OF CHEMISTRY, ACADEMIA SINICA, KUNMING, CHINA. [*Received, November 11th*, 1944.]

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40. *Synthetic Experiments in the B Group of Vitamins. Part I. Riboflavin.*

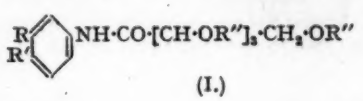
By F. BERGEL, A. COHEN, and J. W. HAWORTH.

A synthesis of *N*-(polyhydroxyalkyl)arylamines is described. Acetylation of an arylamide of an aldonic acid, followed by treatment with phosphorus pentachloride, gives the corresponding imidochloride. Catalytic hydrogenation to an acetylated secondary amine, followed by deacetylation, gives the required *N*-(polyhydroxyalkyl)arylamine.

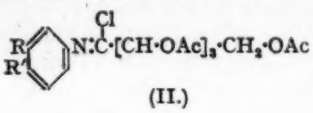
N-(*d*-Ribityl)-*o*-4-xylidine, so prepared, is converted into 6-(*N*-*d*-ribitylamino)-3 : 4-dimethylazobenzene by known methods, and the latter compound undergoes a reductive condensation with alloxantin, yielding riboflavin after complete oxidation of any leuco-riboflavin.

A SYNTHESIS of *N*-(polyhydroxyalkyl)arylamines (III, R″ = H) suitable for the preparation of *iso*alloxazines, including riboflavin, was first described by us in the patent literature [Brit. Pat. 550,169 (6485/41); printed January, 1943], and consisted in converting acetylated arylamides of aldonic acids (cf. I, R″ = Ac) into imidochlorides (II), which were reduced (III, R″ = Ac) and deacetylated to (III, R″ = H). Recently, however, a similar method of preparing *N*-(*d*-ribityl)-*o*-4-xylidine, the intermediate required for the synthesis of riboflavin, was published by Tishler, Wendler, Ladenburg, and Willman (*J. Amer. Chem. Soc.*, 1944, **66**, 1328).

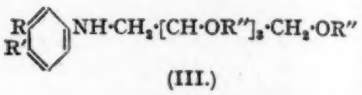
In view of their statement regarding lack of details of our procedure, it is desirable to record a number of experiments on the synthesis of compounds of type (III), R″ = H.



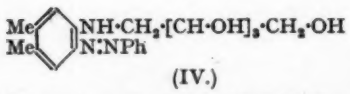
(I.)



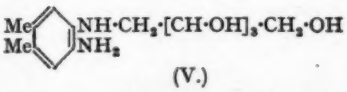
(II.)



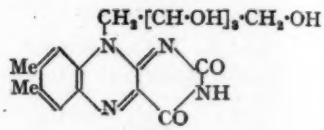
(III.)



(IV.)



(V.)



(VI.)

The conversion of *N*-(*d*-ribityl)-*o*-4-xylidine into riboflavin has long since been reported by Karrer and Meerwein (*Helv. Chim. Acta*, 1935, **18**, 1130; 1936, **19**, 264). They coupled the secondary base with a benzenediazonium salt to form the azo-compound (IV), reduced the latter to the diamine (V), which condensed with alloxan, giving riboflavin (VI). We wish to report a new observation regarding these stages.* The azo-compound (IV) reacted with reduced forms of alloxan, such as alloxantin, in the presence of palladised charcoal with the occurrence of a reductive condensation of (IV), even in the absence of hydrogen. When the reaction was carried out in an atmosphere of nitrogen with an excess of alloxantin, the diamine (V) and alloxan reacted *in situ*; and riboflavin was directly obtained after the nitrogen had been replaced by air to oxidise any leuco-riboflavin.

Returning to the general synthesis of *N*-polyhydroxyalkylarylamines, these experiments were undertaken in order to develop a synthesis of riboflavin in which the *d*-ribityl side chain is introduced into the *iso*alloxazine molecule without the use of the difficulty accessible *d*-ribose. Alternative solutions of this problem have already been reported (see, *e.g.*, Weygand, *Ber.*, 1940, **73**, 1259; B.P. 545,360, 551,491; U.S.P. 2,261,608; Tishler *et al.*, *loc. cit.*) and the present experiments exploit the use of the readily available *d*-arabonolactone.

By adopting the general procedure outlined in the opening paragraph of this paper, the following compounds have been prepared: N-d-*arabityl-aniline*, -p-*toluidine*, -o-4-*xylidine*, and -p-*anisidine*, N-d-*ribityl*-p-*toluidine*, and *N*-*d*-ribityl-*o*-4-xylidine. The characteristics of the last compound were in agreement with those recorded in the literature (Karrer and Meerwein, Tishler *et al.*, *locc. cit.*). When *o*-4-xylidine and *d*-ribonolactone were allowed to react at a higher temperature (above 120°) than was usually employed in the preparation of the substituted anilide, epimerisation was observed and an appreciable amount of *d*-arabono-*o*-4-xylidide was isolated, identical with an authentic specimen prepared from *d*-arabonolactone.

Since the completion of these experiments Work has described (J., 1942, 429) the synthesis of secondary bases by the reduction of imidochlorides derived from certain substituted quinoline-4-carboxyamides, with stannous chloride and ethereal hydrogen chloride. The constitutional factors which determine whether the stannous chloride reduction product is an aldehyde (Sonn and Müller reaction) or a base appear to be uncertain, but it seems fairly clear that the method of catalytic hydrogenation of imidochlorides has wider applicability in the synthesis of secondary amines.

Experimental.

d-*Arabononanilide*.—Following the general method of van Marle (*Rec. Trav. chim.*, 1920, **39**, 549), an intimate mixture of *d*-arabonolactone (1 mol.) and aniline (1 mol.) was heated at 100° for 6 hours. The solid product was powdered, washed with benzene, and crystallised from alcohol, from which d-*arabononanilide* separated in excellent yield, in colourless needles, m. p. 198° (Found: C, 54·9; H, 6·4. $C_{11}H_{15}O_5N$ requires C, 54·8; H, 6·2%).

Tetra-acetyl-d-*arabononanilide*.—*d*-Arabononanilide (2·5 g.) was added gradually to an ice-cooled solution of anhydrous zinc chloride (1·0 g.) in acetic anhydride (15 c.c.). After cooling for 1 hour, the mixture was kept at room temperature for 48 hours and poured into water. The precipitated *tetra-acetyl*-d-*arabononanilide* (3·8 g., m. p. 160°) crystallised from alcohol in colourless needles, m. p. 161° (Found: C, 56·0; H, 5·8. $C_{19}H_{23}O_9N$ requires C, 55·6; H, 5·6%).

N-*Phenyltetra-acetyl*-d-*arabonylimidochloride*.—A mixture of finely powdered tetra-acetyl-*d*-arabononanilide (4·09 g.), phosphorus pentachloride (2·08 g.; *ca.* 1 mol.), and toluene (50 c.c.) was gently heated on the water-bath for 1 hour; the solid gradually dissolved with evolution of hydrogen chloride. Toluene and phosphorus oxychloride were removed under reduced pressure, leaving a yellow oil which solidified on cooling. An ethereal solution of this was filtered clear and treated with light petroleum (b. p. 40—60°); the *imidochloride* then separated in colourless needles (2·4 g.), m. p. 102° (Found: Cl, 8·2. $C_{19}H_{22}O_8NCl$ requires Cl, 8·3%).

N-(*Tetra-acetyl*-d-*arabityl*)*aniline*.—A solution of the above imidochloride (1·5 g.) in ethyl acetate (40 c.c.) was shaken with anhydrous sodium acetate (0·3 g.) and palladised charcoal (25%; 0·2 g.) in a hydrogen atmosphere until no more hydrogen was absorbed. Filtration and evaporation of the solution yielded a yellow oil which solidified on cooling and rubbing. This crystallised from methanol in needles, m. p. 75—76° (Found: C, 57·6; H, 6·1; N, 4·0. $C_{19}H_{25}O_8N$ requires C, 57·7; H, 6·3; N, 3·5%).

N-(d-*Arabityl*)*aniline*.—*N*-(Tetra-acetyl-*d*-arabityl)aniline (1·7 g.) was heated under reflux for ½ hour with a solution of crystalline barium hydroxide (6·0 g.) in water (100 c.c.). Carbon dioxide was passed into the hot solution, barium carbonate removed, the filtrate evaporated to dryness under reduced pressure, and the residue triturated with hot alcohol. N-(d-*Arabityl*)*aniline* (0·5 g.) crystallised in needles, m. p. 157—159°, from the filtered alcoholic solution on cooling (Found: C, 58·2; H, 7·6; N, 6·0. $C_{11}H_{17}O_4N$ requires C, 58·2; H, 7·5; N, 6·2%).

The compounds described below were prepared in a similar manner to that of the analogous compound described above. A better procedure for the preparation of the imidochlorides consisted in heating the toluene suspension of the

* Cf. B.P. 550,836.

corresponding substituted amide with slightly more than 1 mol. of phosphorus pentachloride at 30—50° for ½—1 hour. Toluene and phosphorus oxychloride were removed at 1—2 mm. pressure. The addition of toluene and evaporation under reduced pressure were repeated twice to remove all phosphorus oxychloride and the crude residual imidochloride was usually hydrogenated to the secondary amine without further treatment. (Failure to remove all the phosphorus oxychloride appears seriously to diminish the speed of hydrogenation.) d-*Arabono*-p-*toluidide*, crystallised from alcohol, m. p. 199—200° (Found: N, 5·7. $C_{12}H_{17}O_5N$ requires N, 5·5%); *tetra-acetyl*-d-*arabono*-p-*toluidide*, needles from alcohol, m. p. 167—168° (Found: N, 3·7. $C_{20}H_{25}O_9N$ requires N, 3·3%); N-(p-*tolyl*)*tetra-acetyl*-d-*arabonylimidochloride*, colourless needles, m. p. 82°, from ether–light petroleum (Found: Cl, 8·1. $C_{20}H_{24}O_8NCl$ requires Cl, 8·0%); N-(*tetra-acetyl*-d-*arabityl*)-p-*toluidine*, needles from methanol, m. p. 72° (Found: C, 59·0; H, 6·4; N, 3·6. $C_{20}H_{27}O_8N$ requires C, 58·7; H, 6·6; N, 3·4%); N-(d-*arabityl*)-p-*toluidine*, crystallised from alcohol, m. p. 179° (Found: C, 60·0; H, 7·7; N, 5·9. $C_{12}H_{19}O_4N$ requires C, 59·8; H, 7·9; N, 5·8%).

d-*Ribono*-p-*toluidide*, needles from alcohol, m. p. 157—158° (Found: C, 56·9; H, 6·9. $C_{12}H_{17}O_5N$ requires C, 56·5; H, 6·7%); *tetra-acetyl*-d-*ribono*-p-*toluidide*, needles from alcohol, m. p. 120—121° (Found: N, 3·6. $C_{20}H_{25}O_9N$ requires N, 3·4%); the imidochloride was hydrogenated without complete purification to the acetylated secondary base, which was hydrolysed to N-(d-*ribityl*)-p-*toluidine*, m. p. 138—140° after crystallisation from alcohol (Found: C, 59·8; H, 7·9; N, 5·95. $C_{12}H_{19}O_4N$ requires C, 59·8; H, 7·8; N, 5·8%). *d*-Ribono-*o*-4-xylidide, needles from alcohol, m. p. 160° (Found: N, 5·2. Calc. for $C_{13}H_{19}O_5N$: N, 5·2%); tetra-acetyl-*d*-ribono-*o*-4-xylidide, needles from alcohol, m. p. 112° (Found: N, 3·5. Calc. for $C_{21}H_{27}O_9N$: N, 3·2%); the corresponding imidochloride and acetylated secondary base (m. p. 99°) were obtained by the methods already described, and the latter hydrolysed by barium hydroxide solution or alcoholic sodium hydroxide to *N*-(*d*-ribityl)-*o*-4-xylidine, m. p. 143°, after crystallising from water (56% yield, calculated on *d*-ribonolactone).

d-*Arabono*-o-4-*xylidide*, needles from alcohol or water, m. p. 206° (Found: N, 5·3. $C_{13}H_{19}O_5N$ requires N, 5·2%); *tetra-acetyl*-d-*arabono*-o-4-*xylidide*, prismatic needles from alcohol, m. p. 151° (Found: C, 57·6; H, 6·2; N, 3·4. $C_{21}H_{27}O_9N$ requires C, 57·65; H, 6·2; N, 3·2%); N-(o-4-*xylyl*)*tetra-acetyl*-d-*arabonylimidochloride*, m. p. 83—84° after one crystallisation from ethyl acetate–light petroleum (Found: Cl, 7·4. $C_{21}H_{26}O_8NCl$ requires Cl, 7·8%); N-(*tetra-acetyl*-d-*arabityl*)-o-4-*xylidine*, needles, m. p. 91°, from 80% methanol (Found: C, 59·3; H, 6·9; N, 3·55. $C_{21}H_{29}O_8N$ requires C, 59·7; H, 6·9; N, 3·3%); N-(d-*arabityl*)-o-4-*xylidine*, prisms, m. p. 140—141° (Found: C, 61·0; H, 8·2; N, 5·3. $C_{13}H_{21}O_4N$ requires C, 61·2; H, 8·2; N, 5·5%).

d-*Arabono*-p-*anisidide*, needles from alcohol, m. p. 185—187° (Found: C, 53·1; H, 6·2. $C_{12}H_{17}O_6N$ requires C, 53·0; H, 6·2%); *tetra-acetyl*-d-*arabono*-p-*anisidide*, from alcohol, m. p. 180° (Found: C, 54·5; H, 5·8; N, 3·4. $C_{20}H_{25}O_{10}N$ requires C, 54·8; H, 5·7; N, 3·2%); this compound gave, in the usual manner *via* the imidochloride and subsequent hydrolysis with alcoholic sodium hydroxide, an overall yield of 60% of N-(d-*arabityl*)-p-*anisidine*, m. p. 150° (Found: C, 56·0; H, 7·3; N, 5·4. $C_{12}H_{19}O_5N$ requires C, 56·2; H, 7·4; N, 5·4%).

Epimerisation in the Preparation of d-*Ribono*-o-4-*xylidide*.—A mixture of equimolecular amounts of *d*-ribonolactone and *o*-4-xylidine was heated at 130° for 5 hours, and the product extracted with boiling butanol and filtered. *d*-Ribono-*o*-4-xylidide, m. p. 158—160° (cf. above), crystallised from the filtrate. The butanol-insoluble fraction was crystallised from alcohol, yielding (about 35%) *d*-arabono-*o*-4-xylidide, m. p. 205°, which was not depressed in admixture with an authentic specimen prepared from *d*-arabonolactone.

Synthesis of Riboflavin from Alloxantin and 6-(N-d-*Ribitylamino*)-3 : 4-*dimethylazobenzene*.—The azo-compound was prepared by coupling diazotised aniline with *N*-(*d*-ribityl)-*o*-4-xylidine (cf. Karrer, *Helv. Chim. Acta*, 1935, **18**, 1130). A mixture of it (0·5 g.) and alloxantin (2·0 g.) with palladised charcoal (0·2 g.; 10%) in N-alcoholic hydrogen chloride (5 c.c.) and alcohol (80 c.c.) was shaken in an atmosphere of nitrogen at 60—70° for 5 hours. The nitrogen was then displaced by air, and agitation continued for 4 hours at room temperature. The catalyst, mixed with crude riboflavin, was filtered off, and extracted with a mixture of water (15 c.c.) and N-sodium hydroxide (1 c.c.). The filtered alkaline solution was acidified with acetic acid and riboflavin was soon precipitated as an orange-yellow solid (0·15 g.), m. p. 280°. Crystallisation from aqueous acetic acid raised the m. p. to 282° (corr.) (Found: C, 54·0; H, 5·45; N, 15·0. Calc. for $C_{17}H_{20}O_6N_4$: C, 54·4; H, 5·3; N, 14·9%).

We are grateful to Mr. E. G. Hughes for information concerning the *p*-anisidine derivatives, and to Mr. J. D. H. Kirkland for assistance in the experimental work.

RESEARCH DEPARTMENT, ROCHE PRODUCTS LTD., WELWYN GARDEN CITY. [*Received, October 3rd*, 1944.]

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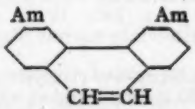
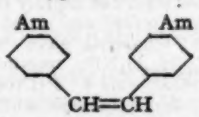
41. *Phenanthrene-3 : 6-diamidine.*

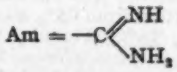
By H. J. BARBER and C. E. STICKINGS.

A synthesis of phenanthrene-3 : 6-diamidine is described, and its trypanocidal action reported.

Phenanthrene-3 : 6-diamidine (I) is structurally related to *cis*-stilbene-4 : 4'-diamidine (II) (J., 1943, 2), which has a trypanocidal action similar to that of the *trans*-isomer ("Stilbamidine"). This diamidine has now been prepared and preliminary indications are that its trypanocidal activity is slight.

(I.) 



(II). Am = 

Phenanthrene-3 : 6-dinitrile, required for the preparation of the diamidine (I), has not been described, nor has the corresponding dinitro- or dibromo-phenanthrene, either of which would be a suitable intermediate. The literature on substitution in the phenanthrene (or hydrophenanthrene) series contra-indicated attempts at direct nitration or bromination and equally at introduction of other substituents readily convertible into nitrile groups, *e.g.*, NH:C·CCl_3, CH_2Cl, CHO. Since the conversion Br→CN by means of cuprous cyanide is generally preferable to the route NO_2→NH_2→CN, 3 : 6-*dibromophenanthrene* was selected as the intermediate to be obtained by the Pschorr method.

4-Bromo-2-nitrobenzaldehyde has been prepared by oxidation of 4-bromo-2-nitrotoluene by amyl nitrite (Rottig, *J. pr. Chem.*, 1935, **142**, 35). 4-Bromo-2-nitrotoluene was prepared by nitration of *p*-toluidine sulphate (Ullmann and Dootson, *Ber.*, 1918, **51**, 9), followed by a Sandmeyer reaction. Attempts to repeat the oxidation with amyl nitrite gave very low yields; manganese dioxide, *p*-nitrosodimethylaniline and bromine were tried without success, but reaction with chromic acid in acetic acid–anhydride was a workable method, although the yield was only 17—18%.

The Perkin condensation, reduction, and Pschorr ring-closure presented no difficulties, but the *3 : 6-dibromophenanthrene-9-carboxylic acid* could not readily be purified. Attempts to decarboxylate the crude acid by repeated sublimation or by the action of copper chromite in quinoline gave poor results. Simultaneous conversion into dinitrile and loss of carbon dioxide occurred when the sublimed acid was heated with cuprous cyanide in boiling quinoline.

The iminoether hydrochloride was prepared in chloroform by the usual method, and the crude iminoether base isolated and converted directly into the amidine isethionate. As this salt was too soluble for convenient isolation, the hydrochloride was precipitated, and crystallised from hydrochloric acid.

Toxicity and trypanocidal tests (*T. equiperdum* in mice) gave the following results:

	L.D.$_{50}$.	E.D.$_{50}$.	C.D.$_{50}$.	Chemotherapeutic index.
Intravenous injection	0·03 mg./g.	0·0075 mg./g.	—	—
Subcutaneous injection	0·14 mg./g.	0·005 mg./g.	0·05 mg./g.	3

(E.D.$_{50}$: mean effective dose—trypanosomes cleared from peripheral blood after 3 days.
C.D.$_{50}$: mean curative dose—trypanosomes cleared from peripheral blood for 28 days or longer.)

Experimental.

All analyses are semi-micro.

4-Bromo-2-nitrobenzylidene Diacetate.—4-Bromo-2-nitrotoluene (20 g.; 0·087 g.-mol.) was dissolved in glacial acetic acid (40 c.c.) and acetic anhydride (220 c.c.), and sulphuric acid (21 c.c.; 0·25 g.-mol.) added with stirring. The whole was cooled to 5°, and a solution of chromium trioxide (25 g.; 0·25 g.-mol.) in water (15 c.c.) and glacial acetic acid (100 c.c.) added during 30 minutes at 5—10°. The mixture was stirred for a further 30 minutes, then poured into ice-water (1·5 l.). The product was collected, washed until the filtrate was colourless, and dried in a vacuum; yield, 12 g. The *diacetate*, after crystallising from alcohol, then twice from methanol, gave white rhombs, m. p. 133—136° (Found: Br, 24·0. $C_{11}H_{10}O_4NBr$ requires Br, 24·1%).

4-Bromo-2-nitrobenzaldehyde.—Crude 4-bromo-2-nitrobenzylidene diacetate (12 g.) was boiled for 1½ hours with alcohol (100 c.c.) and 2N-sulphuric acid (100 c.c.). The solution, after cooling, was treated with water (350 c.c.). The aldehyde was extracted with ether, and the extract washed with water, evaporated to 100 c.c., shaken with saturated sodium bisulphite solution (50 c.c.), and kept overnight. The bisulphite compound was collected, washed with ether, dissolved in warm water (60 c.c.), and decomposed with 2N-sodium carbonate (100 c.c.). The aldehyde was collected, washed with water, and dried in a vacuum; light yellow solid, m. p. 95—97°; yield, 3·7 g. (17·5%, based on the 4-bromo-2-nitrotoluene used).

Sodium 4-Bromophenylacetate.—4-Bromophenylacetonitrile (prepared from 4-bromobenzyl bromide by the method of Wislicenus and Elvert, *Ber.*, 1908, **41**, 4121) was hydrolysed in 50% sulphuric acid in the usual way, and converted into the sodium salt.

cis-*4 : 4′-Dibromo-2′-nitrostilbene-α-carboxylic Acid.*—4-Bromo-2-nitrobenzaldehyde (6·9 g.; 0·03 g.-mol.), sodium 4-bromophenylacetate (7·2 g.; 0·03 g.-mol.), and acetic anhydride (50 c.c.) were heated together at 105—115° for 22 hours with occasional shaking. The excess of acetic anhydride was decomposed with water at 100—120°, and water then added. After cooling, the liquid was decanted, and the sticky residue dissolved in ether and washed with water. On extraction of the ethereal solution with 2N-aqueous ammonia, three layers were obtained, the lowest one solidifying on long standing, and the two lower layers forming a single one on warming (the lowest layer was probably the sparingly soluble ammonium salt). The ammoniacal extract was warmed for complete solution, and poured into dilute hydrochloric acid. The crude orange solid thus obtained was collected and washed with water; m. p. 180—190°. On crystallisation from glacial acetic acid (130 c.c.)–water (25 c.c.) the *acid* was obtained as orange rods, m. p. 204—206°; yield, 12·8 g. (52%) (Found: Br, 37·4; N, 3·3. $C_{15}H_9O_4NBr_2$ requires Br, 37·4; N, 3·3%).

cis-*4 : 4′-Dibromo-2′-aminostilbene-α-carboxylic Acid.*—Ferrous sulphate ($FeSO_4,7H_2O$) (12·5 g.; 0·045 g.-mol.) was dissolved in water (50 c.c.) on the steam-bath, and a mixture of aqueous ammonia (*d* 0·880) (25 c.c.) and water (25 c.c.) added. To the hot suspension of ferrous hydroxide was added immediately a solution of *cis*-4 : 4′-dibromo-2′-nitrostilbene-α-carboxylic acid (2·13 g.; 0·005 g.-mol.) in warm 2N-aqueous ammonia (10 c.c.). After heating for 1½ hours on the steam-bath, the mixture was filtered hot, with the aid of charcoal and kieselguhr. The residue was repeatedly extracted with boiling dilute aqueous ammonia, until no precipitate was produced on acidification of the filtrate with acetic acid (about four extractions); in some cases it was necessary to refilter with charcoal to remove colour and iron. The combined extracts were warmed (to dissolve crystals of the ammonium salt) and made acid to litmus with acetic acid. The acid came down as a bright yellow solid but rapidly turned white on shaking for a few minutes. After cooling, the crude material was filtered, washed with water and dried in a vacuum; m. p. 188—191°; yield, 1·75 g. (87%). Recrystallisation from 65% alcohol (25 vols.) (charcoal) gave the *acid* as brownish-white narrow plates, m. p. 192—194°; yield, 1·55 g. (78%) (Found: Br, 40·1. $C_{15}H_{11}O_2NBr_2$ requires Br, 40·3%).

3 : 6-Dibromophenanthrene-9-carboxylic Acid.—*cis*-4 : 4′-Dibromo-2′-aminostilbene-α-carboxylic acid (1·0 g.; 0·0025 g.-mol.) was suspended in alcohol (15 c.c.), and sulphuric acid (0·3 c.c.; 0·0055 g.-mol.) added with shaking. After a few minutes the sulphate crystallised. The thick paste was stirred and cooled to room temperature, and amyl nitrite (0·6 c.c.; 0·0045 g.-mol.) added all at once with stirring. The practically clear solution after a few minutes began to deposit feathery yellow crystals. After an hour these changed to a fine heavy yellow powder (in one experiment this change did not occur).

Calcium hypophosphite (4·25 g.; 0·25 g.-mol.) in hot water (35 c.c.) was stirred with sodium carbonate (3·2 g. of monohydrate; 0·26 g.-mol.) in hot water (25 c.c.), a trace of copper bronze added to the filtered solution, and the temperature adjusted to about 50°. The suspension of diazonium salt was poured in during 2 minutes with stirring, and the mixture heated for 15 minutes on the steam-bath. The brown solid was collected, washed with water, and dried in the oven. The crude acid was thus obtained as a brown powder; yield, 0·85 g. (88%). In a number of experiments the

yield varied from 70 to 90%. For analysis, a small quantity was crystallised from chlorobenzene, the *acid* being obtained as a brown powder, m. p. 290—292° (Found : Br, 42·3. $C_{15}H_8O_2Br_2$ requires Br, 42·1%).

3 : 6-*Dibromophenanthrene.*—(A) Crude 3 : 6-dibromophenanthrene-9-carboxylic acid (0·85 g.) was dissolved in ether (500 c.c.) and filtered from copper, and the ether evaporated. The residue was sublimed at 250°/1 mm., giving a yellowish-white sublimate, m. p. 260° upwards. This was resublimed, m. p. about 280°, with sintering. The product was largely soluble in alkali; yield, 0·35 g.

(B) The sublimed material was added to quinoline (5 c.c.) at 210—220°, containing copper chromite catalyst. After heating for 10 minutes, the solution was cooled somewhat and poured into concentrated hydrochloric acid (50 c.c.), boiled, filtered, washed with water, and dried at 90°. The black powder was sublimed at 180—190°/1 mm., and the white sublimate crystallised from petrol, from which there separated white needles, m. p. 188—191°.

A repetition of this experiment, using unsublimed acid, gave a low yield of less pure *material*, m. p. 183—188° (Found : Br, 47·2. $C_{14}H_8Br_2$ requires Br, 47·6%).

Phenanthrene-3 : 6-*dinitrile.*—Crude 3 : 6-dibromophenanthrene-9-carboxylic acid (4·4 g.) was sublimed at 260—290°/1 mm., the yellowish-white sublimate (1·85 g.) mixed with cuprous cyanide (1·14 g.) and added to boiling quinoline (6 c.c.) during 5 minutes, and the solution boiled for a further 30 minutes. After cooling somewhat, the mixture was poured into concentrated hydrochloric acid (100 c.c.), boiled, filtered, washed with more acid, and then with water. The grey solid was washed with cold sodium hydroxide solution (to remove unchanged acid and phenolic compounds), and then with water, and dried at 90°. The crude material was sublimed at 220—230°/0·6 mm., to give fine, slightly yellow needles; 0·55 g. (50%) (overall yield from amine, 16—17%). Recrystallisation from glacial acetic acid (60 vols.) gave a 76% return of the *nitrile* as long white needles, m. p. 257—259° (Found : N, 12·15. $C_{16}H_8N_2$ requires N, 12·3%).

The preparation was also tried with unsublimed acid, but yields were lower still; in one case no nitrile was isolated.

Phenanthrene-3 : 6-*diamidine.*—The method described in B.P. 559,015 was used. The *dihydrochloride* crystallised from dilute hydrochloric acid in white needles; yield, 41% (Found : N, 14·6; Cl, 18·15. $C_{16}H_{14}N_4,2HCl,3H_2O$ requires N, 14·4; Cl, 18·25%).

The authors wish to express their indebtedness to Mr. P. G. Hickson for assistance in the preparative work, to Mr. S. Bance, B.Sc., for the semi-micro analyses, to the Biological Division of Messrs. May and Baker Ltd. for the biological results, and to the Directors of Messrs. May and Baker Ltd. for permission to publish the results.

MESSRS. MAY AND BAKER LTD., DAGENHAM, ESSEX. [*Received, November 14th*, 1944.]

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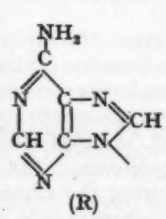
42. *The Structure of Adenosine Di- and Tri-phosphates.*

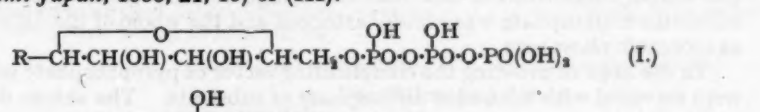
By J. MASSON GULLAND and E. O'FARRELL WALSH.

The existing experimental evidence for the constitutions of adenosine di- and tri-phosphates leaves some doubt as to the exact disposition of their acid-labile phosphoryl groups. The action of cold aqueous alkali and of the phosphatases of Russell's viper venom on these compounds has been investigated and the results are discussed in relation to the possible structures. Lohmann's conclusions are confirmed.

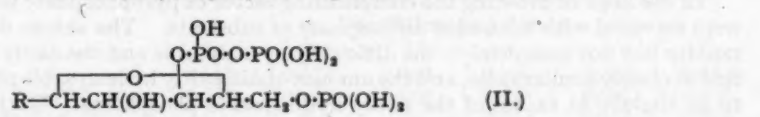
THE structure of adenosine triphosphate, first isolated in 1929 (Lohmann, *Naturwiss.*, **17**, 624; Fiske and Subbarow, *Science*, **70**, 381), has long been a matter of dispute, and the point of attachment of the labile pyrophosphoryl group to the adenosine-5-phosphate is not yet known with certainty. The existence of inosine triphosphate as a deamination product of adenosine triphosphate (Kleinzeller, *Biochem. J.*, 1942, **36**, 729) proves conclusively that the amino-nitrogen of the adenine is not involved, and therefore the structure proposed by Barrenscheen and Filz (*Biochem. Z.*, 1932, **256**, 115) need not be considered. The pyrophosphoryl residue must therefore be united with adenosine-5-phosphate either through the stable 5-phosphoryl group as in (I) (Lohmann, *Biochem. Z.*, 1932, **254**, 381; 1935, **282**, 120) or through one of the hydroxyl groups at C_2 or C_3 of the ribose as in (II) (Satoh, *J. Biochem. Japan*, 1935, **21**, 19) or (III).



(R)



(I.)



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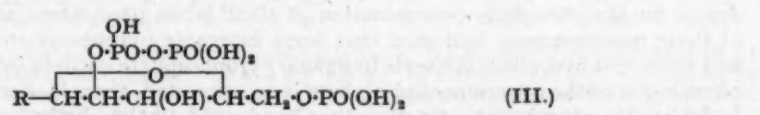


(III.)

Lohmann's formula is based on the results of electrometric titrations of adenosine di- and tri-phosphoric acids before and after acid hydrolysis, and on the behaviour of the compound towards hydrolytic reagents. Alkaline hydrolysis with baryta yielded adenosine-5-phosphate and inorganic pyrophosphoric acid, and N-acid at 100° " easily hydrolysed " two of the phosphoric acid residues at a rate closely similar to that of hydrolysis of inorganic pyrophosphate under similar conditions. In this communication the terms " easily hydrolysable " (acid labile) and " difficultly hydrolysable " (acid stable) phosphorus are used in accordance with Lohmann's definition.

The ability of adenosine triphosphate to form a soluble copper complex with dilute copper sulphate and lime water and to give a positive Böeseken reaction with boric acid (Lohmann, *loc. cit.*; Makino, *Biochem. Z.*,

1935, **278**, 161; Barrenscheen and Jachimowicz, *ibid.*, 1937, **292**, 350), thus resembling adenosine-5-phosphate and differing from adenosine-3-phosphate (Klimek and Parnas, *ibid.*, 1932, **252**, 392; *Z. physiol. Chem.*, 1933, **217**, 75), offers strong support for Lohmann's formula in which the adjacent hydroxyl groups at C_2 and C_3 are unesterified. Lohmann points out, however, that these reactions are not fully understood and that the results are not clearly predictable in the case of a compound containing in its molecule a congestion of hydroxyl groups and an amino-group.

The structure (II) was inferred by Satoh from the results of enzyme experiments. He observed that non-specific phosphatases, having no pyrophosphatase activity under the conditions of experiment, split off one-third of the total phosphorus from adenosine triphosphate as inorganic phosphoric acid and left the organic pyrophosphate as inosine pyrophosphate, deamination having occurred simultaneously with dephosphorylation. Pyrophosphatases, on the other hand, removed half the pyrophosphate phosphorus as inorganic orthophosphate, *i.e.*, one-third of the total phosphorus, yielding an adenosine diphosphoric acid, which was isolated as the calcium salt. This compound was dephosphorylated by non-specific phosphomonoesterase but was not attacked by pyrophosphatase. In agreement with Satoh, Barrenscheen and others (Barrenscheen and Lang, *Biochem. Z.*, 1932, **253**, 406; Barrenscheen and Jachimowicz, *ibid.*, 1937, **292**, 350) observed that bone phosphatase mineralised one-third of the total phosphorus of adenosine triphosphate, the inorganic phosphate originating almost entirely from the difficultly hydrolysable part, but Liebknecht (*ibid.*, 1939, **303**, 96) disagreed with Barrenscheen and claimed that bone phosphatase liberated the labile phosphorus first.

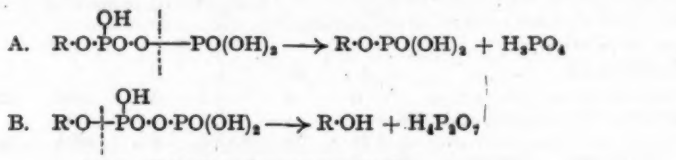
We have investigated the action of cold alkali on adenosine di- and tri-phosphates under the same conditions as those that effect the cleavage of yeast ribonucleic acid to its component nucleotides. Excess of N-sodium hydroxide acting on adenosine triphosphate at 20° for 24 hours liberated inorganic pyrophosphate but no inorganic orthophosphate. In the case of adenosine diphosphate under the same conditions, the alkali liberated half the total phosphorus as inorganic orthophosphate. These results suggested that the labile pyrophosphoryl group of adenosine triphosphate and the labile phosphoryl group of the diphosphate might be linked to muscle adenylic acid by an alkali-unstable ester link resembling the alkali-labile internucleotide linkage of yeast ribonucleic acid (Gulland and Walsh, following paper); in that case, adenosine triphosphate could have a structure (III) analogous with that of Satoh but differing from the triphosphoric acid structure of Lohmann. In order to test this hypothesis and in the hope of confirming or disproving one or other of the above formulæ, we have investigated the action of the 5-nucleotidase of Russell's viper venom (Gulland and Jackson, *Biochem. J.*, 1938, **32**, 590) on adenosine di- and tri-phosphates before and after cold alkaline hydrolysis. This enzyme has a high affinity for adenosine-5-phosphate, which is rapidly dephosphorylated, but does not attack other organic phosphates in the normal conditions of enzymic experiments.

The venom dephosphorylated adenosine triphosphate at a rapid rate, comparable with that of its action on adenosine-5-phosphate under similar conditions, but the rate diminished and action ceased when about 20% of the total phosphorus had been liberated as inorganic phosphate. Determinations of the easily hydrolysable phosphorus by heating with N-hydrochloric acid at 100° for 7 minutes (Lohmann, *loc. cit.*; Ferdmann, *Z. physiol. Chem.*, 1933, **216**, 205) indicated that most of the liberated phosphate originated from the difficultly hydrolysable part. When, however, the venom acted on adenosine triphosphate which had previously been subjected to cold alkaline hydrolysis, less phosphate was liberated, although the conditions of experiment were strictly comparable. From this, it was inferred that inorganic pyrophosphate, set free during the enzyme action or by the pretreatment with cold alkali, inhibited the 5-nucleotidase. Experiments with muscle adenylic acid and the venom in the presence of inorganic pyrophosphate confirmed this conclusion, and when the venom concentration was sufficiently high relative to the amount of inhibiting pyrophosphate present, adenosine triphosphate was rapidly attacked and the whole of the difficultly hydrolysable phosphorus liberated as inorganic phosphate.

In the hope of avoiding the complicating factor of pyrophosphate inhibition of the enzyme, the experiments were repeated with adenosine diphosphate as substrate. The venom dephosphorylated adenosine diphosphate rapidly but not completely; the difficultly hydrolysable and the easily hydrolysable phosphorus were mineralised at closely similar rates, and the amount of difficultly hydrolysable phosphorus set free as phosphate appeared to be slightly in excess of the easily hydrolysable phosphorus. During the experiment, samples were withdrawn for the phosphate determination of alkali-labile phosphorus and acid-labile phosphorus. The results of these measurements indicated that some inorganic pyrophosphate was produced during the experiment, and since acid hydrolysis converts inorganic pyrophosphate entirely into orthophosphate whereas only half the phosphorus of the adenosine-diphosphate is so converted, there is, during the experiment, an increase in easily hydrolysable phosphorus. On the other hand, cold alkaline hydrolysis liberates as phosphate half the phosphorus of the adenosine diphosphate but does not appreciably attack inorganic pyrophosphate in the same conditions. It follows that the observed difference between the amounts of acid-labile and alkali-labile phosphorus is equivalent to the amount of inorganic pyrophosphate, and therefore to twice the increase in easily hydrolysable phosphorus, produced by the enzyme. The necessary correction can thus be made when calculating the relative proportions of easily- to difficultly-hydrolysable phosphate liberated by the venom. Having regard to the limits of accuracy of the experiment, this ratio was very nearly 1 : 1.

When the venom was incubated with adenosine diphosphate which had been previously subjected to cold alkaline hydrolysis, the remaining organic phosphate was rapidly and completely mineralised by the 5-nucleotidase.

These results can only be explained on the basis of Lohmann's formula for adenosine diphosphate (corresponding to I). Adenosine diphosphate suffers hydrolysis by the enzyme in two ways, represented by A and B:



(where R is the adenosine radical)

The main reaction (A) involves splitting of the pyrophosphate link with liberation of inorganic orthophosphate and muscle adenylic acid, which is at once hydrolysed by the 5-nucleotidase to adenosine and inorganic phosphate. The subsidiary reaction (B) produces inorganic pyrophosphate but no phosphate.

It is therefore concluded that the two phosphoryl groups in adenosine diphosphate are united as pyrophosphate, and since both labile phosphoryl groups of adenosine triphosphate are also united as pyrophosphate, Lohmann's formula (I) is correct. Whilst this work was in progress, further evidence that adenosine triphosphate is a derivative of triphosphoric acid has been furnished by Needham and his collaborators (*J. Gen. Physiol.*, 1944, **27**, 355) from their studies on myosin.

The support for the correctness of Lohmann's formula (I) for adenosine triphosphate provided in this communication has a bearing on the structure of codehydrogenase II, which was originally suggested (v. Euler and Schlenk, *Z. physiol. Chem.*, 1937, **246**, 64) as being a derivative of adenosine triphosphate. That view cannot, however, be reconciled with the conversion of codehydrogenase I into codehydrogenase II by phosphorylation in ether (Schlenk, *Naturwiss.*, 1937, **25**, 668) or with the facts that codehydrogenase II contains no readily hydrolysable phosphate and yields no alkaline degradation product active as cophosphorylase (Schlenk, Högberg, and Tingstam, *Arkiv Kemi, Min., Geol.*, 1939, 13A, No. 11). Support is thus lent to Schlenk's formulation (Symposium on Respiratory Enzymes, 1942, 104, University of Wisconsin Press) of codehydrogenase II as a derivative of adenosine diphosphate with an additional phosphoryl monoester group, and not as a derivative of adenosine triphosphate.

Experimental.

The adenosine triphosphate used was a sample of the barium salt, prepared from horse muscle. It had a N : P ratio of 5 : 3 and gave a positive Böeseken reaction, and 68% of the total phosphorus was hydrolysed to inorganic orthophosphate by N-hydrochloric acid at 100° in 7 minutes. It was further purified by washing with ice-cold water, acidified to pH 4 with dilute acetic acid, in order to remove any traces of adenylic acid and adenosine diphosphate.

Adenosine diphosphate was prepared from the triphosphate either by the action of rabbit muscle myosin (Greenstein and Edsall, *J. Biol. Chem.*, 1940, **133**, 397) as described by Bailey (*Biochem. J.*, 1942, **36**, 121), or by the action of yeast hexokinase (Meyerhof, *Biochem. Z.*, 1927, **183**, 186) in the presence of glucose according to the method of Colowick and Kalckar (*J. Biol. Chem.*, 1943, **148**, 121).

Inorganic orthophosphate was determined by Briggs's modification (*J. Biol. Chem.*, 1922, **53**, 13) of the Bell–Doisy colorimetric method.

Action of Cold Alkali on Adenosine Diphosphate and Triphosphate.—Neutral solutions of the sodium salts of adenosine di- and tri-phosphate were prepared as follows: Barium adenosine di- or tri-phosphate (*ca.* 20 mg.) was dissolved in a few c.c. of ice-cold water, acidified with a few drops of dilute hydrochloric acid, and sodium sulphate (*ca.* 10 mg.) added. The solution, freed from barium sulphate by centrifuging, was neutralised to phenolphthalein by the addition of dilute alkali, and the volume adjusted to 20 c.c. with ice-cold water. Samples (1·0 c.c.) were taken for the determinations of total phosphorus and easily hydrolysable phosphorus, *i.e.*, phosphorus liberated as inorganic phosphate by N-hydrochloric acid at 100° in 7 minutes. For the determination of alkali-labile phosphorus, samples (1·0 c.c.) were mixed with water (2·0 c.c.) and N- or 4N-sodium hydroxide (1·0 c.c.) and left for 24 hours at 20°.

	Adenosine triphosphate.			Adenosine diphosphate.		
	Phosphorus, mg. per c.c.					
Expt. No.	1	2	3	4	5	6
Total	0·112	0·073	0·096	0·082	0·132	0·132
Inorganic phosphate after 7 mins. N-HCl at 100°	0·075	0·049	0·065	0·042	0·067	0·067
Inorganic phosphate after 24 hrs. 1% NaOH at 20°	0	0	0	0·023	0·031	0·034
Inorganic phosphate after 24 hrs. N-NaOH at 20°	0	0	0	0·040	0·064	0·066

Action of Cold Alkali on Inorganic Pyrophosphate.—A freshly prepared solution of potassium pyrophosphate (1·10 g.) in cold water (500 c.c.) had a total phosphorus concentration of 0·414 mg. per c.c., of which 0·0027 mg. was present as orthophosphate. Samples (1·0 c.c.) were mixed with water (2·0 c.c.) and N- or 4N-sodium hydroxide (1·0 c.c.) and kept at 20° in a closed tube for 24 hours. After neutralisation, the orthophosphate present was determined.

P as orthophosphate.	% total P.
Original solution	0·65
After hydrolysis with 1% NaOH	1·69
After hydrolysis with N-NaOH	2·66

The total phosphorus concentration used was higher than in the other experiments, otherwise the amount of orthophosphate would have been too small to permit accurate determination.

Action of Russell's Viper Venom on Adenosine Triphosphate.—The results of two experiments, A and B, are recorded. A mixture (15 c.c.) of sodium adenosine triphosphate [from 20 mg. (A) and 30 mg. (B) of barium salt], Michaelis' veronal buffer (5 c.c.), Russell's viper venom [5 mg. (A) and 15 mg. (B)], and water was incubated in the presence of toluene at 37° and pH 8·6. The total phosphorus concentrations were 0·096 (A) and 0·143 (B) mg. per c.c. Samples (1·0 c.c.)

were withdrawn at intervals for the determination of inorganic phosphate, and simultaneously, samples (1·0 c.c.) were withdrawn, heated in a closed tube with 2N-hydrochloric acid (1·0 c.c.) for 7 minutes in the boiling water-bath, and the inorganic phosphate determined.

Time in minutes.	Inorganic phosphate as % of total phosphorus.									
	0.		15.		30.		60.		120.	
Experiment.	A.	B.	A.	B.	A.	B.	A.	B.	A.	B.
I. Phosphate liberated by enzyme action ...	0	0	19·5	28	20·4	32	22·0	35	22·6	35·5
II. Phosphate liberated by enzyme and acid hydrolysis	68	68	85·5	94	86·1	98	86·7	100	86·7	100
III. Acid-stable phosphate liberated by enzyme (II—68)	0	0	17·5	26	18·1	30	18·7	32	18·7	32
IV. Easily hydrolysable phosphate liberated by enzyme (I—III)	0	0	2·0	2	2·3	2	3·3	2	3·9	3·5

An experiment was carried out under conditions of phosphorus, buffer and enzyme concentrations identical with Expt. A, but using as substrate adenosine triphosphate which had been previously subjected to the action of N-sodium hydroxide at 20° for 24 hours. After 30 minutes at 37° and pH 8·6, only 13·9% of the total phosphorus was present as inorganic orthophosphate as compared with 20·4% in experiment A.

Effect of Inorganic Pyrophosphate on 5-Nucleotidase of Russell's Viper Venom.—A mixture (10 c.c.) of muscle adenylic acid (5 mg.), veronal buffer (5 c.c.), venom (3 mg.), and water was incubated in the presence of toluene at 37° and pH 8·6. The total phosphorus concentration was 0·045 mg. per c.c. Parallel experiments containing in addition potassium pyrophosphate in 0·01, 0·001 and 0·0001 M concentration were simultaneously carried out. Samples (2·0 c.c.) were withdrawn at intervals for the determination of inorganic orthophosphate.

Time, mins.	Dephosphorylation, %.			
	0.	0·01.	0·001.	0·0001M-P_2O_7''''.
0	0	0	0	0
15	93	2	52	85
30	95	4	80	95
60	98	7	92	98

The above quantities are corrected for the amount of orthophosphate produced by a weak pyrophosphatase activity of the venom demonstrable when potassium pyrophosphate and venom are included under identical conditions but without muscle adenylic acid as substrate.

Action of Russell's Viper Venom on Adenosine Diphosphate.—A mixture (15 c.c.) of sodium adenosine diphosphate (from 25 mg. of barium salt), veronal buffer (5 c.c.), venom (5 mg.), and water was incubated with toluene at 37° and pH 8·6. The total phosphorus concentration was 0·085 mg. per c.c. Samples (1·0 c.c.) were withdrawn at intervals for the determination of inorganic phosphate. Simultaneously, samples (1·0 c.c.) were withdrawn, heated in a closed tube with 2N-hydrochloric acid (1·0 c.c.) in a boiling water-bath for 7 minutes, and the inorganic phosphate determined. Samples (1·0 c.c.) were also mixed with 4N-sodium hydroxide (1·0 c.c.) and water (2·0 c.c.) containing a few drops of 0·5M-potassium cyanide to arrest enzyme action (Gulland and Walsh, *loc. cit.*), and the mixtures were kept at 20° for 24 hours, neutralised, and the inorganic phosphate determined.

	Inorganic phosphate as % of total phosphorus.							
	A.	B.	C.	D.	E.	F.	G.	H.
Time, mins.	Phosphate liberated by enzyme action.	After 7 mins. N-HCl at 100°.	After 24 hrs. N-NaOH at 20°.	Apparent stable P set free (B—51).	Apparent labile P set free (A—D).	P present as P_2O_7'''' (B—C).	Stable P set free by venom (corrected).	Labile P set free by venom (corrected).
0	0	51	—	0	0	—	0	0
15	27·6	64	60·6	13	14·6	3·4	11·3	16·3
30	41·4	73·1	69·9	22·1	19·3	3·2	20·5	20·9
60	53·7	80·8	74·3	29·8	23·9	6·5	26·6	27·1

The corrected values for stable phosphorus liberated as phosphate by the enzymes (G) are calculated by subtracting half the inorganic pyrophosphate phosphorus (F) from the apparent acid-stable phosphorus liberated (D). The corrected values for acid-labile phosphorus liberated as phosphate by the enzymes (H) are obtained by difference from A and G.

Action of Russell's Viper Venom on the Products of Cold Alkaline Hydrolysis of Adenosine Diphosphate.—A solution (2·0 c.c.) of sodium adenosine diphosphate, of total phosphorus concentration 0·14 mg. per c.c., was mixed with 4N-sodium hydroxide (0·6 c.c.), and the mixture kept at 20° for 24 hours. The excess of alkali was neutralised to pH 8·6 with dilute sulphuric acid, veronal buffer (2 c.c.) and venom (2 mg.) added, and the mixture, adjusted to 5 c.c., incubated with toluene at 37° and pH 8·6 for 30 minutes. Samples (2·0 c.c.) were withdrawn for the determination of inorganic orthophosphate. The inorganic orthophosphate, expressed as percentage of total phosphorus, was 49·2% before enzyme action began and 98·7% after 30 minutes.

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UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, October 30th*, 1944.]

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43. *The Constitution of Yeast Ribonucleic Acid. Part IX. Alkali-labile Linkages.*

By J. MASSON GULLAND and E. O'FARRELL WALSH.

Evidence has now accumulated that yeast ribonucleic acid does not contain phospho-diester groups involving the hydroxyl at C_5 of the sugar. The suggestion, previously made tentatively, cannot be sustained, namely, that the observed liberation of inorganic phosphate by Russell's viper venom occurred as a result of the united action

of its phosphodiesterase and highly specific 5-nucleotidase on such groups. The explanation of the dephosphorylation is found in the combined results of fission of phospho-monoesters (i) by a very slow enzyme action and (ii) by alkaline hydrolysis. Thus, enzymic experiments have permitted the demonstration of the presence in yeast ribonucleic acid of alkali-labile ester groups, of which the existence has hitherto been inferred by reason of the alkaline fission of the acid to nucleotides. The site of the labile linkages in the polynucleotide is discussed and considered to be at C_3 of the sugar.

During the first, rapid stage of enzymic dephosphorylation, the liberated phosphate originated from the purine nucleotides. Subsequently, both purine and pyrimidine nucleotide phosphates were set free, the latter more rapidly than the former.

RUSSELL'S viper venom, which contained a phosphodiesterase and 5-nucleotidase but no apparent non-specific phosphomonoesterase (Gulland and Jackson, *Biochem. J.*, 1938, **32**, 590, 597), effected partial dephosphorylation of yeast ribonucleic acid (Gulland and Jackson, J., 1938, 1492). The possibility was stated tentatively that the nucleic acid might contain doubly esterified phosphoryl groups linked to hydroxyls at C_3 and C_5 of the sugar radicals, and that these groups were set free as inorganic phosphate by 5-nucleotidase following hydrolysis of the C_3 link by the diesterase. It was, however, pointed out that a decision on this point would have to be deferred until knowledge became available of the action of 5-nucleotidase on nucleoside-5-phosphates other than muscle adenylic and inosinic acids, the only substrates known for this highly specific enzyme (Gulland and Jackson, *Biochem. J.*, 1938, **32**, 597).

Evidence against the presence of phosphoryl groups at C_5 in yeast ribonucleic acid has accumulated from two directions. First, uridine-5-phosphate and guanosine-5-phosphate, both possible substrates on the preceding line of argument, were prepared by Gulland and Hobday (J., 1940, 746) and are not attacked by 5-nucleotidase. Second, the products of hydrolysis of the nucleic acid by cold 1% sodium hydroxide solution are the 3-phospho-esters guanylic, adenylic, cytidylic and uridylic acids. It is, however, a sound assumption that, if 5-phospho-ester groups were present in the molecule, they would resemble the 3-phospho-esters in surviving this treatment, since adenosine-5-phosphate, for example, is resistant to cold 1% sodium hydroxide solution and is only slightly more susceptible to drastic conditions of alkaline hydrolysis than is adenosine-3-phosphate (Gulland and Jackson, J., 1938, 1492). It thus seems that yeast ribonucleic acid does not contain 5-phospho-ester groups and that the explanation of the dephosphorylation by Russell's viper venom must be sought in other directions.

In the present investigation, made with purified yeast ribonucleic acid from two B.D.H. samples, measurements of inorganic phosphate were made (i) at intervals during the action of the venom on the purified nucleic acid; (ii) at intervals during the action of the venom on the mixed nucleotides resulting from the hydrolysis of the acid by cold 1% sodium hydroxide solution; (iii) after the action of cold 1% sodium hydroxide solution on the products formed when the venom acts on the acid for various periods of time.

The venom liberated about 25% of the total phosphate from the nucleic acid with relative rapidity. The rate then slackened, but dephosphorylation continued steadily for several days and finally appeared to cease when 50—55% of the total phosphate had been mineralised. The slow liberation of phosphate in the second stage proceeded at a rate closely similar to that of the dephosphorylation under comparable conditions of the mixed nucleotides produced by cold alkaline hydrolysis of the same quantity of nucleic acid. It was concluded that in addition to its pronounced 5-nucleotidase and phospho-diesterase activities the venom also exhibited a very weak or slow phosphomonoesterase activity towards the nucleotides, and this was confirmed by experiments with the mixed nucleotides and with guanylic, adenylic, cytidylic, and uridylic acids.

When sodium hydroxide, in amounts sufficient to make a 1% solution, was added to the products of the action of venom on purified nucleic acid, inorganic phosphate was set free in addition to that liberated during the enzyme action. This was not due to the further action of the venom phosphatases, since it occurred in presence of cyanide ions, which were shown to inhibit the action of these enzymes on a variety of substrates, as will be described elsewhere. Since phosphate was not liberated by cold 1% sodium hydroxide solution in control experiments with the nucleic acid or the mixed 3-phospho-nucleosides, it follows that alkali-unstable phospho-esters were formed during the action of the venom on the nucleic acid. These tended to accumulate during the early stage of the venom action and later underwent hydrolysis, either gradually in the alkaline (pH 8·6) medium of the experiments or more rapidly in 1% sodium hydroxide solution. By the end of the period of enzymic hydrolysis, the quantity of alkali-labile esters in the solution had become extremely small.

These facts suggest that, using as a basis of discussion a polymer of the hypothetical tetranucleotide (Fletcher, Gulland, and Jordan, J., 1944, **33**), one or both of the diester groups associated with each four atoms of phosphorus is in the form (I), where A represents an alkali-unstable link and B the alkali-stable 3-phospho-ester

(I.)

link found in the individual nucleotides as obtained by alkaline hydrolysis of the nucleic acid. Enzymic fission could occur entirely at B in one such group or concurrently at A and B in both groups; the resulting ester groups with the A link unattacked would then undergo further hydrolysis by the alkali.

This liberation of inorganic phosphate by alkali after inhibition of the enzymes with cyanide forms the first demonstration of the independent existence of alkali-unstable phosphoryl groups in the fission products

of yeast ribonucleic acid. Their presence in the acid itself has for many years only been inferred from the ease with which alkaline hydrolysis effects fission into the four constituent nucleotides.

The following considerations are relevant in assigning positions to these groups in the samples under investigation. Yeast ribonucleic acid is a polynucleotide considerably larger than a tetranucleotide (Loring, *J. Biol. Chem.*, 1939, **128**, *Sci. Proc.*, **33**, 61; Fischer, Böttger, and Lehmann-Echternacht, *Z. physiol. Chem.*, 1941, **271**, 246; Fletcher, Gulland, Jordan, and Dibben, J., 1944, 30). The hydroxyls at C_3 (presence of phosphoryl group) and at C_5 of the sugar radicals are excluded. The hydroxyls of the purines and pyrimidines are not substituted, since they were titratable (Fletcher, Gulland, and Jordan, J., 1944, **33**). The amino-groups were unsubstituted, since they underwent deamination without diminution of the molecular size (Fletcher, Gulland, Jordan, and Dibben, *loc. cit.*). It thus seems that the hydroxyls at C_2 of the sugars alone remain as possible sites, a view which is not novel (Levene and Tipson, *J. Biol. Chem.*, 1935, **109**, 623; Makino, *Z. physiol. Chem.*, 1935, **236**, 201; Bredereck, "Fortschritte d. Chemie Org. Naturstoffe," 1938, **1**, 152), although previous conjectures were based on the hypothesis that the molecule is a simple tetranucleotide. This view cannot be accepted unreservedly until positive, rather than negative, evidence becomes available, since so far as we are aware the literature does not record for substituents in the hydroxyls of sugars differences in stability so marked in degree as to explain the complete fission of an ester at C_2 whilst a similar linkage at C_3 remains wholly unattacked.

A working hypothesis is as follows: Pentose polynucleotides, which suffer alkaline fission into nucleotides and of which the molecular weight is not diminished by deamination, are built up by a series of phospho-ester linkages at C_2 and C_3 of the sugars. Alkali-labile phospho-amide groups may occur in some samples of nucleic acids, guanine-uridylic acid, for example, being obtainable from some, but not all, samples of yeast ribonucleic acid (Falconer, Gulland, Hobday, and Jackson, J., 1939, 907; Bredereck, Berger, and Richter, *Ber.*, 1941, **74**, 338), but such groups would undergo fission and deamination by nitrous acid (Falconer *et al.*, *loc. cit.*; Gulland, *Chem. and Ind.*, 1940, **59**, 312; Fischer, *Naturwiss.*, 1942, **30**, 377) and diminution of molecular size would then occur. It is possible that phospho-amide linkages may unite polynucleotides of intermediate size to form large molecules of the nucleic acid in its native state; if so, they might undergo, or survive, hydrolysis in the alkaline media at present used to extract the acid from yeast.

The phosphate of yeast nucleic acid or of a mixture of its nucleotides may be estimated differentially as purine nucleotide phosphate and pyrimidine nucleotide phosphate by the method of Jones (*J. Biol. Chem.*, 1916, **24**, *Sci. Proc.* iii). During the action of Russell's viper venom on the acid, samples were analysed by his method for the amounts of purine and pyrimidine nucleotide phosphate remaining in organic combination. During the first stage of the enzyme action (comparatively rapid dephosphorylation) all the pyrimidine nucleotide phosphate originally present remained combined, *i.e.*, the phosphate liberated, about 25% of the total, originated from the purine nucleotides. During the second stage (slow dephosphorylation) both purine and pyrimidine nucleotide phosphate were set free, the latter more rapidly than the former. The phosphate liberated during this stage resulted from the alkaline hydrolysis of the alkali-labile phosphoryl groups and the action of the non-specific phosphomonoesterase on the nucleotides present.

The integration of results of this nature with analogous observations of others (for example, Bolomey and Allen, *J. Biol. Chem.*, 1942, **144**, 113; Bredereck, Berger, and Richter, *Ber.*, 1941, **74**, 338) may in time throw light on the relative orientation of the nucleotides in the polynucleotide.

Experimental.

Two samples of B.D.H. nucleic acid were used; one was obtained from Fletcher, Gulland, and Jordan (*loc. cit.*), the other was purified as described by these authors. Estimations of inorganic phosphate were made colorimetrically by the Bell–Doisy–Briggs method.

Action of Russell's Viper Venom on Purified Yeast Ribonucleic Acid and on the Mixed Nucleotides obtained by Cold Alkaline Hydrolysis.—Substrate A: Purified yeast ribonucleic acid (P = 9·2%) (0·2 g.) was dissolved in a little water with sufficient aqueous sodium hydroxide to yield a solution faintly pink to phenolphthalein, and the solution diluted with water to 20 c.c. Substrate B: The same sample of nucleic acid (0·2 g.) was dissolved as before, 10% sodium hydroxide solution (2 c.c.) added, and the whole made up to 20 c.c. with water. After 24 hours at 20°, glacial acetic acid was added until the solution was faintly pink to phenolphthalein. Enzyme solution: Russell's viper venom (100 mg.) in water (10 c.c.). Mixtures of substrate solutions A and B respectively (2·0 c.c.), Clark and Lubs pH 8·6 borate buffer (10 c.c.) and water (5 c.c.) were warmed to 37°, enzyme solution (2·0 c.c.) added to each, and the volumes adjusted to 20 c.c. A few drops of toluene were added, and the mixtures incubated at 37° and pH 8·6. The phosphorus concentrations were respectively: Expt. A, 0·086 mg. per c.c.; Expt. B, 0·083 mg. per c.c. Samples (1·0 or 2·0 c.c.) were withdrawn during the course of the incubation for the determination of inorganic phosphate.

Table I.

Time, hours.		0.	2.	5.	8.	26.	50.	75.	100.	120.
PO_4 liberated, %.	A	0	6·1	13·2	17·2	27·5	33·6	39·4	46·1	49·8
,, ,,	B	0	0	0	+	6·2	10·5	16·0	20·5	28·0

No free phosphate was liberated from the mixed nucleotides during the first 5 hours and only a trace was detected after 8 hours' incubation, but the quantity was too small to permit accurate determination. This apparently delayed action of the non-specific phospho-monoesterase in the venom is a definite characteristic and has been observed in numerous experiments carried out with various concentrations of enzyme and substrate. Enzymic hydrolysis then proceeds steadily for several days, after which time the activity appears to increase. This increase in activity of the enzyme after prolonged incubation with the substrate is also characteristic and similar curves have been obtained in numerous

experiments. It is hoped to discuss possible explanations elsewhere; toluene was present throughout the experiments and in no case was bacterial contamination observed.

Action of Russell's Viper Venom on the Individual Nucleotides of Yeast Ribonucleic Acid.—Solutions of the sodium salts of each of the four nucleotides were incubated separately with borate buffer (7·5 c.c.) and Russell's viper venom (15 mg.) at 37° and pH 8·6 in the presence of toluene, the volumes being 15 c.c., and phosphorus concentration 0·082 mg. per c.c. in each case. Samples (2·0 c.c.) were withdrawn for the determination of inorganic phosphate. Solutions of the substrates and buffer incubated at 37° and pH 8·6 without enzyme liberated no phosphate during the time of the experiment.

TABLE II.

Phosphate liberated, %.

Time, hours.	Yeast adenylic.	Guanylic.	Cytidylic.	Uridylic.	Time, hours.	Yeast adenylic.	Guanylic.	Cytidylic.	Uridylic.
0	0	0	0	0	93	16·5	28·5	22·5	7·3
40	6·9	15·8	10·6	0	113	19·0	32·7	25·2	10·1
66	11·7	22·6	17·0	3·6	164	25·0	41·0	33·6	15·2

The Action of Cold Aqueous 1% Sodium Hydroxide on the Products of the Action of Russell's Viper Venom on Purified Yeast Ribonucleic Acid.—A mixture (20 c.c.) of the acid (P = 9·2%) (*ca.* 20 mg.), dissolved in water with sufficient aqueous sodium hydroxide to effect solution, Clark and Lubs borate buffer (10 c.c.), Russell's viper venom (20 mg.), and water was incubated in the presence of toluene at 37° and pH 8·6. The phosphorus concentration was 0·0997 mg. per c.c. Samples (1·0 or 2·0 c.c.) were withdrawn for the estimation of inorganic phosphate (Table III, col. A).

As each sample was taken for immediate determination of phosphate, a similar sample was at once diluted with 1 vol. of 4% sodium hydroxide solution and 2 vols. of water, a few drops of 0·5M-cyanide added, and the alkaline solution kept at 20° for 24 hours in a tightly corked tube. After neutralisation of the excess of alkali, the inorganic phosphate was determined by the usual procedure (Table III, col. C). After 22½ hours and 49½ hours samples (1 c.c.) were also taken, and phosphatase action arrested by addition of cyanide; the samples were then incubated at 37° and pH 8·6 for 24 hours, and the phosphate determined (Table III, col. B).

TABLE III.

Phosphate liberated, %.

Time, hours.	A.	B.	C.	Time, hours.	A.	B.	C.
0	0	0	0	49½	34·5	37·8	45·1
4	9	—	12	73½	42·7	—	49·5
8	15	—	19	120	53	—	54
22½	25·5	27·7	32·7				

Ratio of Purine to Pyrimidine Nucleotide Phosphate set free by Russell's Viper Venom acting on Purified Yeast Ribonucleic Acid.—A mixture (25 c.c.; P, 0·100 mg. per c.c.) of the acid (*ca.* 28 mg.), dissolved in a little water and sufficient dilute alkali to effect solution, borate buffer (15 c.c.), venom (20 mg.), and water was incubated with toluene at pH 8·6 and 37°. Samples (1·0 or 2·0 c.c.) of the above mixture were withdrawn at intervals for the determination of inorganic phosphate. Simultaneously two 1 c.c. samples were taken and mixed with an equal volume of 2N-hydrochloric acid; one was heated for 1 hour, the other for 2 hours, at 100°. The inorganic phosphate in each was then determined. All purine nucleotide phosphorus is hydrolysed completely to inorganic phosphate by heating in N-acid for 1 hour at 100°, whereas the pyrimidine nucleotides are but slowly attacked. The amount of pyrimidine nucleotide phosphorus set free per hour under these conditions is a constant (Jones, *loc. cit.*), so that the amount set free during the 1-hour hydrolysis is equal to that set free during the second hour of the 2-hour hydrolysis, *i.e.*, (2 hr. value − 1 hr. value). The difference between this quantity and the 1-hour value is equal to the sum of the purine nucleotide phosphorus in organic combination and the phosphorus present as inorganic phosphate, *i.e.*, [1 hr. value—(2 hr. value—1 hr. value)]. The pyrimidine nucleotide phosphorus remaining in organic combination can therefore be calculated from the expression Total phosphorus—[1 hr. value—(2 hr. value—1 hr. value)].

In this way the amounts of purine and pyrimidine nucleotide phosphate present in organic combination in the enzyme–nucleic acid mixture may be determined throughout the enzyme action. It follows that the phosphate set free by the venom may be differentiated into phosphate of purine and of pyrimidine nucleotide origin.

TABLE IV.

Inorganic phosphate expressed as percentage of total phosphorus present in the mixture.

Time, hours.	0.	8.	22.	50.	76.	118.	140.
I. Phosphate set free by enzyme action	0	16	23	31·1	37·9	49·7	54
II. Total purine phosphate and free phosphate [1 hr. value—(2 hr. value—1 hr. value)]	49·7	—	49·7	55·4	59·3	65·2	68·1
III. Remaining pyrimidine phosphate (total P—II)	50·3	—	50·3	44·6	40·7	34·8	31·9
IV. Pyrimidine phosphate set free by enzyme action (total pyrimidine P—III)	0	0	0	5·7	9·6	15·5	18·4
V. Purine phosphate set free by enzyme action (I—IV)	0	16	23	25·4	28·3	34·2	35·6

It is a pleasure to acknowledge our indebtedness to the Government Grant Committee of the Royal Society and to Imperial Chemical Industries Ltd. for assistance.

UNIVERSITY COLLEGE, NOTTINGHAM.

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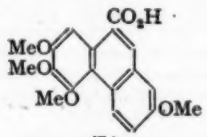
44. *Colchicine and Related Compounds. Part V. The Structure of Windaus's Deaminocolchinol Methyl Ether.*

By Norman Barton, J. W. Cook, and J. D. Loudon.

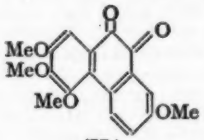
Deaminocolchinol methyl ether, obtained by Windaus by exhaustive methylation of colchinol methyl ether, is not a tetramethoxy-9-methylphenanthrene as he believed. It is an unsaturated compound containing one ethylenic linkage, and gives on oxidation with chromic acid an unsaturated *ketone* and 2 : 3 : 4 : 7-*tetramethoxyphenanthraquinone*. The formation of this quinone establishes the methoxylation pattern of colchinol methyl ether, and hence the positions of five of the substituents in the ring system of colchicine.

Colchinol methyl ether has been converted by a variety of routes into deaminocolchinol methyl ether, which is usually (perhaps invariably) accompanied by an isomeric iso*deaminocolchinol methyl ether*; both isomerides are hydrogenated to the same *dihydride*. By stepwise oxidation, deaminocolchinol methyl ether and its isomeride have been converted into 2 : 3 : 4 : 7-tetramethoxy-10-phenanthraldehyde and -9-phenanthraldehyde, respectively. These transformations show that deaminocolchinol methyl ether and its isomeride have the structures (XII) and (XIII).

In Part IV (Buchanan, Cook, and Loudon, J., 1944, 325) the syntheses of 2 : 3 : 4 : 6- and 2 : 3 : 4 : 7-tetramethoxy-9-methylphenanthrene were described and it was shown that, contrary to the views of Windaus (*Annalen*, 1924, **439**, 59), neither of these compounds was identical with deaminocolchinol methyl ether, an important degradation product of colchicine. The synthetic work did not, however, distinguish the 2 : 3 : 4 : 7-isomer from 2 : 3 : 4 : 5-tetramethoxy-9-methylphenanthrene, since these two compounds were obtained from the corresponding 9-carboxylic acids (acid-A, m. p. 236°, and acid-B, m. p. 185°), which were simultaneous products of a Pschorr reaction and were not individually oriented. This distinction has now been made. 2-Nitro-5-methoxybenzaldehyde was condensed with sodium 3 : 4 : 5-trimethoxyphenylacetate, the *product* reduced, and the resulting *amino-acid* converted into 2 : 3 : 4 : 7-*tetramethoxyphenanthrene*-10-*carboxylic acid* (I). Oxidation of this acid furnished 2 : 3 : 4 : 7-*tetramethoxyphenanthraquinone* (II), which was characterised by the *diazine* derived from *o*-phenylenediamine. The same quinone and diazine were also obtained in similar fashion from acid-A (corresponding to the tetramethoxy-9-methylphenanthrene, m. p. 116—117°; Part IV), whereas acid-B yielded quite distinct *products*. Accordingly acid-A is (III) and in Part IV the A-series of compounds has the 2 : 3 : 4 : 7-, and the B-series has the 2 : 3 : 4 : 5-tetramethoxyphenanthrene structure. Incidentally it may be noted that the alternative method of orientation based on decarboxylation of the 9- and the 10-acid to the parent phenanthrene is probably here subject to complications, for Pschorr found (*Annalen*, 1912, **391**, 40) that dry distillation of 3 : 4 : 5-trimethoxyphenanthrene-9-carboxylic acid produced the corresponding methyl ester and we have encountered a similar case in 2 : 3 : 4 : 6-tetramethoxyphenanthrene-9-carboxylic acid, which was converted into its methyl ester when slowly distilled in presence of copper in a high vacuum.



(I.)



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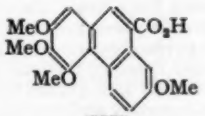
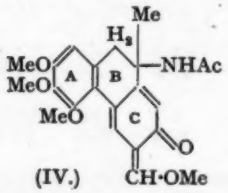
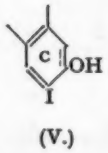


(III.)

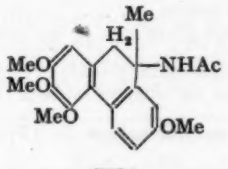
When oxidised with sodium dichromate in acetic acid, deaminocolchinol methyl ether yielded a quinone identical with (II) and distinct from 2 : 3 : 4 : 6-*tetramethoxyphenanthraquinone* prepared for comparison from 2 : 3 : 4 : 6-tetramethoxyphenanthrene-9-carboxylic acid. This result is of considerable importance—by establishing the methoxylation pattern of *N*-acetylcolchinol methyl ether and thereby defining the position of the phenolic group in ring C of *N*-acetylcolchinol, it removes the existing ambiguity regarding the positions of substituents in ring C of colchicine itself and, at the same time, confirms the arrangement of methoxyl groups in ring A. In terms of the Windaus formulation colchicine accordingly becomes (IV), *N*-acetyliodocolchinol (V) and *N*-acetylcolchinol methyl ether (VI).



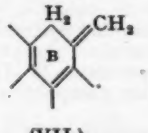
(IV.)



(V.)



(VI.)

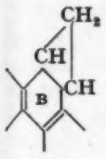


(VII.)

Deaminocolchinol methyl ether is produced by Hofmann degradation of colchinol methyl ether (Windaus, *loc. cit.*) or by elimination of acetamide from the *N*-acetyl derivative (Part III; Cook and Graham, J., 1944, 322). It is not only distinct from 2 : 3 : 4 : 7-tetramethoxy-9-methylphenanthrene, but differs from this and from the other synthetic isomerides in two significant respects. It gives no sign of picrate formation when treated with picric acid in methanol, whereas under similar conditions the synthetic compounds immediately give red solutions from which the picrates separate. Secondly, it is readily hydrogenated to a *dihydride*

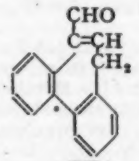
in presence of a palladium catalyst, under conditions which leave the synthetic compounds and also *N*-acetylcolchinol methyl ether unchanged. These facts indicate that deaminocolchinol methyl ether does not contain a phenanthrene arrangement of double bonds and, together with the oxidation to 2 : 3 : 4 : 7-tetramethoxyphenanthraquinone, suggest the alternative structures 2 : 3 : 4 : 7-tetramethoxy-9- or -10-methylene-9 : 10-dihydrophenanthrene (*e.g.*, VII). The further implications of these formulæ are not, however, borne out by the chemical behaviour of the compound. It is not, as would be expected, readily isomerised to an aromatic structure. For instance, in course of its preparation it survives moderately intense conditions of heat and alkalinity (see Experimental) and it was recovered unchanged after 3 hours' boiling with sodium methoxide in methanol. It was also recovered, although in diminished quantity, after heating with a mixture of hydrochloric and acetic acids. Further, the dihydride has not the properties expected of a 9- or 10-methyl-9 : 10-dihydrophenanthrene, for it resists dehydrogenation with palladium and with selenium under conditions considerably more severe than suffice to effect a rapid conversion of 9 : 10-dihydrophenanthrene into phenanthrene. These objections to structure (VII) for deaminocolchinol methyl ether and to the reduced form for its dihydride are essentially the same as the objections previously raised against the Windaus formula for *N*-acetylcolchinol methyl ether (Part I; Cohen, Cook, and Roe, J., 1940, 194). In general, the formulation of ring B as six-membered in these and similar degradation products of colchicine implies a facile aromatisation which is not found in practice.

In Part I it was shown that colchinol methyl ether in reaction with nitrous acid yielded a carbinol which from its stability must be either primary or secondary. Although the point was not finally settled, failure to obtain an aldehyde or corresponding acid on oxidation, together with the behaviour of the carbinol with phthalic anhydride, indicated that it is probably a secondary alcohol. We have now found that the carbinol is strongly lævorotatory and that on dehydration it yields a mixture of products from which deaminocolchinol methyl ether and an isomeric substance, *isodeaminocolchinol methyl ether*, have been isolated. Re-investigation showed that a small quantity of the *iso*-compound is also produced together with deaminocolchinol methyl ether during the elimination of acetamide from *N*-acetylcolchinol methyl ether and it is possible that the same compound was formed but escaped detection in the earlier Hofmann degradations of colchinol methyl ether. The new product resembles its isomeride in its failure to form a picrate and in its ability to undergo hydrogenation with a palladium catalyst, whereby from both isomerides the same dihydride is produced.

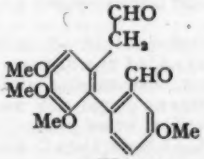


(VIII.)

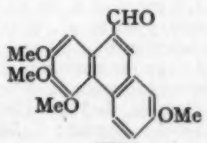
Since their properties preclude an aromatic structure for the isomerides, these hydrogenation results cannot be interpreted in terms of a 6-membered ring B, except by assigning to one of the isomerides a fused *cyclo*propane structure (VIII) and improbabilities are incurred in regard to both its formation and its subsequent unilateral reduction to the dihydride of (VII). On the other hand, the more accommodating possibilities of a 5- and 7-membered ring B are not at first sight in accord with a simple oxidation of deaminocolchinol methyl ether to 2 : 3 : 4 : 7-tetramethoxyphenanthraquinone. The quinone, however, is not the only product of this oxidation, for a second *product*, $C_{19}H_{18}O_5$, having properties suggestive of an αβ-unsaturated ketone was also isolated. Such a product could be accommodated almost equally well in a 6- or 7-membered ring B and even in a 5-membered ring B, although here perhaps with less acceptance because of the separation of the oxidised methylene group from the aromatic nucleus. At the same time, in view of the ease with which diphenyl triketone is oxidised to benzil in an acid medium (Schönberg and Azzam, J., 1939, 1428), it suggests one possible route by which an appropriate dibenz*cyclo*heptatriene might be converted into the phenanthraquinone (II). An actual instance of the latter type of reaction, although the mechanism remains obscure, is recorded by Weitzenböck (*Monatsh.*, 1913, **34**, 199), who obtained phenanthraquinone from the compound (IX) by oxidation with chromic acid in acetic acid.



(IX.)



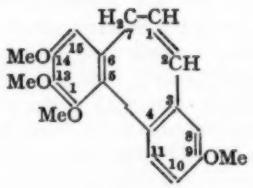
(X.)



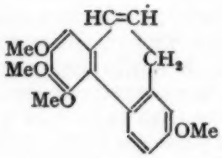
(XI.)

In order to secure more precise information attention was next turned to the controlled stepwise oxidation of the olefinic centre in deaminocolchinol methyl ether. The compound was largely unaffected by hydrogen peroxide in *tert.*-butyl alcohol with osmium tetroxide as catalyst (cf. Milas and Sussman, *J. Amer. Chem. Soc.*, 1936, **58**, 1302), but it readily afforded a *glycol*, $C_{19}H_{22}O_6$, by Criegee's method using osmium tetroxide in ether (*Annalen*, 1936, **522**, 77). Fission of the glycol by means of lead tetra-acetate in benzene (Criegee, *Ber.*, 1931, **64**, 260; Criegee, Kraft, and Rank, *Annalen*, 1933, **507**, 159) yielded a gum which slowly crystallised to a monoaldehyde, $C_{19}H_{18}O_5$. The latter must be 2 : 3 : 4 : 7-*tetramethoxy*-10-*phenanthraldehyde* (XI), since on oxidation with permanganate it gave the corresponding acid indistinguishable from the synthetic acid (I) and affording the same *methyl* ester. The production of the 10-aldehyde in this way strongly indicates the intermediate formation of the dialdehyde (X) and it may be added in confirmation of this view that the reluctance to solidify shown by the crude gum is immediately overcome by warming with a trace of sodium carbonate in methanol. Finally, a similar series of oxidations was carried out with *iso*deaminocolchinol methyl ether.

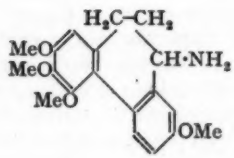
In this case, because of the small amount of material available, the crystalline product corresponding to (but distinct from) the above glycol was not fully characterised, but was oxidised directly with lead tetra-acetate and gave 2 : 3 : 4 : 7-tetramethoxy-9-phenanthraldehyde identical with a synthetic specimen (Part IV) and yielding the same *oxime*.



(XII.)



(XIII.)



(XIV.)

These results appear to us to show conclusively that deaminocolchinol methyl ether is 9 : 12 : 13 : 14-tetramethoxy-3 : 4 : 5 : 6-dibenz-$\Delta^{1:3:5}$-*cyclo*heptatriene (XII) * and that *iso*deaminocolchinol methyl ether is 9 : 12 : 13 : 14-tetramethoxy-3 : 4 : 5 : 6-dibenz-$\Delta^{3:5:7}$-*cyclo*heptatriene (XIII). This conclusion is not necessarily in conflict with the isolation by Windaus (*loc. cit.*) of a small amount of 9-methylphenanthrene from deaminocolchinol methyl ether, by demethylation, followed by zinc dust distillation. Contraction of the 7-membered ring to a 6-membered ring might well have taken place under the drastic conditions of zinc dust distillation, as has been pointed out previously (Part I). It might even have occurred during the prior demethylation with boiling hydriodic acid (compare Cook, J., 1928, 62). The ketone which we obtained by chromic acid oxidation of deaminocolchinol methyl ether (XII) is evidently formed by oxidation of the methylene group at position 7. As mentioned above, this ketone may be an intermediate in the formation of the quinone (II). It is possible, nevertheless, that the ketone and the quinone represent different paths of oxidation, and that in the formation of the quinone the initial attack is on the ethylenic linkage, as in the stepwise conversion of (XII) into tetramethoxyphenanthrenecarboxylic acid (I).

If it is assumed that the Hofmann deamination of colchinol methyl ether to (XII) is unaccompanied by rearrangement of the carbon skeleton, an assumption that seems well founded (compare Stevens and Richmond, *J. Amer. Chem. Soc.*, 1941, **63**, 3132), the further conclusion may be drawn that colchinol methyl ether also contains a 7-membered ring, carrying an amino-substituent (*e.g.*, XIV); the precise location of the amino-group requires further investigation. While it would be premature to assume the presence of a *cyclo*heptane system in colchicine itself, yet the extensive degradations of the alkaloid carried out by Windaus are not inconsistent with such a structure. In particular, it may be remarked that the oxidation of colchicine to succinic acid (Windaus, *loc. cit.*, and *Sitzungsber. Heidelberg. Akad. Wiss., Math.-Nat. Kl. A*, 1914, 18 Abh.), which is difficult to reconcile with formula (IV), is readily explicable on the basis of a structure corresponding with (XIV). We are continuing the investigation, with special reference to the implications of our present results.

Experimental.

2-Nitro-5-methoxy-α-(3′ : 4′ : 5′-trimethoxyphenyl)cinnamic Acid.—Sodium 3 : 4 : 5-trimethoxyphenylacetate (Part III, *loc. cit.*) (19·1 g.; dried at 130°), 2-nitro-5-methoxybenzaldehyde (Mason, J., 1925, **127**, 1195) (13·9 g.), and acetic anhydride (190 c.c.) were heated at 125—130° for 8 hours. After addition of water and cautious warming to decompose acetic anhydride the mixture was thoroughly extracted with ether. The product partly separated in the process and was combined with the remainder, which was recovered from the ethereal extract by shaking with aqueous sodium carbonate, followed by acidification. *2-Nitro-5-methoxy-α-(3′ : 4′ : 5′-trimethoxyphenyl)cinnamic acid* (55% yield) formed yellow needles (from methanol); the m. p. was at first 137°, and later changed spontaneously to 158—159° (Found : C, 58·8; H, 4·7. $C_{19}H_{19}O_8N$ requires C, 58·6; H, 4·9%).

2-Amino-5-methoxy-α-(3′ : 4′ : 5′-trimethoxyphenyl)cinnamic Acid.—A solution of the nitro-acid (15·9 g.) in concentrated aqueous ammonia (64 c.c.) and water (250 c.c.) was added to a mixture of ferrous sulphate (110 g.), water (340 c.c.), and concentrated aqueous ammonia (285 c.c.) maintained, with stirring, at 70°. After 2 hours the filtrate and washings from the iron hydroxide were acidified, and the precipitated *amino-acid* was crystallised from ethanol, forming masses of colourless needles, m. p. 189—190°, which became yellow when pressed on porous plate, and gave yellow solutions in ethanol (yield, 75%) (Found : C, 63·6; H, 6·0. $C_{19}H_{21}O_8N$ requires C, 63·5; H, 5·85%).

2 : 3 : 4 : 7-Tetramethoxyphenanthrene-10-carboxylic Acid (I).—N-Sodium nitrite (34 c.c.) was added at 5° to a solution of the amino-acid (11·3 g.) in 2·5N-sulphuric acid (113 c.c.) and sufficient acetic acid to give a clear solution when warmed. After dilution with water (400 c.c.), the resulting diazo-solution was neutralised with sodium carbonate and heated at 50° until a coupling test was negative. Tarry matter which separated was redissolved by addition of dilute sodium hydroxide solution and, after cooling, the solution was acidified. The precipitated *acid* (I) crystallised from dilute ethanol in small, pale yellow needles, m. p. 200° (Found : C, 66·6; H, 5·3. $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%), and with ethereal diazomethane gave a *methyl* ester, which, after distillation in a high vacuum (bath temperature, 245°), crystallised from methanol in colourless prisms, m. p. 103—104° (Found : C, 67·5; H, 5·55. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6%). After the ester had distilled, a higher fraction was obtained (bath at 250—290°) which, after repeated crystallisation from methanol, formed brown plates, m. p. 210·5—211° (Found : C, 63·7; H, 5·45; N, 8·3%). This *compound*, which was insoluble in sodium bicarbonate solution but soluble in sodium hydroxide solution, had already been obtained

* We adopt the system of numbering used by Kenner and Turner (J., 1911, **99**, 2104; compare Kenner, J., 1913, **103**, 613, and Taurinš, *J. pr. Chem.*, 1939, **153**, 192) for dibenz*cyclo*heptatriene. Patterson and Capell ("The Ring Index," New York, 1940, p. 280) suggest a different system, which seems less suitable, as it involves different schemes of numbering for the two isomeric dibenz*cyclo*heptadienes. Moreover, as Kenner and Turner point out, it is logical to number first all the carbon atoms of the 7-membered ring, if the compounds are named as derivatives of *cyclo*heptane.

by extraction of a chloroform solution of the crude acid (I) with sodium hydroxide after the acid itself had been extracted with sodium carbonate. It possibly corresponded with a similar *compound*, m. p. 159—160°, which had been isolated in the preparation of 2 : 3 : 4 : 6-tetramethoxyphenanthrene-9-carboxylic acid (Part IV, *loc. cit.*; compare Sharp, J., 1936, 1235) (Found : C, 63·7; H, 5·7; N, 8·7%). These by-products, neither of which gave a colour with ferric chloride in alcoholic solution, have not been investigated further.

2 : 3 : 4 : 7-*Tetramethoxyphenanthraquinone* (II).—(*a*) A solution of 2 : 3 : 4 : 7-tetramethoxyphenanthrene-10-carboxylic acid (0·3 g.) in boiling acetic acid (3 c.c.) was treated with a solution of sodium dichromate (0·6 g.) in water (0·3 c.c.) and acetic acid (0·6 c.c.). After being heated under reflux for ½ hour and then diluted with water (25 c.c.), the mixture was extracted with chloroform. The extract was washed with dilute sulphuric acid and then dilute sodium carbonate solution (which removed a small amount of organic acid), dried, and evaporated. A solution of the residue in benzene–ligroin (3 : 2) was passed through a column of alumina, from which a dark red band was eluted with benzene. The eluate gave the *quinone* (II) as red-violet needles or deep violet prisms (from benzene–ligroin), m. p. 193—194° (Found : C, 66·2; H, 5·0. $C_{18}H_{16}O_6$ requires C, 65·9; H, 4·9%). A solution of this quinone in hot acetic acid, treated with a warm solution of *o*-phenylenediamine in methanol, gave a *diazine* which crystallised from methanol in lemon-yellow needles, m. p. 176—177° (Found : C, 72·0; H, 4·8; N, 6·8. $C_{24}H_{20}O_4N_2$ requires C, 72·0; H, 5·0; N, 7·0%).

(*b*) The same quinone and diazine, identified by mixed m. p.'s, were obtained from acid-A (III) (m. p. 236°; Part IV, *loc. cit.*). In this case the diazine was obtained in two interconvertible forms, *viz.*, the lemon-yellow needles, m. p. 176—177°, and orange needles, m. p. 185—186°. The m. p. of the lemon-yellow form changed to the higher value on cooling and remelting.

2 : 3 : 4 : 5-*Tetramethoxyphenanthraquinone*, fan-shaped clusters of red needles, m. p. 120—122°, was obtained similarly from acid-B (m. p. 185°; Part IV) (Found : C, 66·05; H, 5·0. $C_{18}H_{16}O_6$ requires C, 65·9; H, 4·9%). The corresponding *diazine* formed orange prisms, micro-m. p. 143° * (Found : N, 7·0. $C_{24}H_{20}O_4N_2$ requires N, 7·0%). An acidic by-product of the oxidation, probably 4 : 5 : 6 : 6′-*tetramethoxydiphenic acid*, m. p. 214—216° (decomp.), was recovered from the sodium carbonate washings (Found : C, 59·8; H, 4·85. $C_{18}H_{18}O_8$ requires C, 59·7; H, 5·0%).

2 : 3 : 4 : 6-*Tetramethoxyphenanthraquinone*, prepared by similar oxidation of 2 : 3 : 4 : 6-tetramethoxyphenanthrene-9-carboxylic acid (Sharp, *loc. cit.*), crystallised from benzene–ligroin in two interconvertible forms, (i) long orange needles, m. p. 184°, and (ii) red rods, micro-m. p. 193°; admixture with 2 : 3 : 4 : 7-tetramethoxyphenanthraquinone (II) gave an indefinite m. p. *ca.* 180°, after sintering (Found : C, 65·9; H, 4·9. $C_{18}H_{16}O_6$ requires C, 65·9; H, 4·9%). The corresponding *diazine* formed pale lemon-yellow crystals, m. p. 180—181°, depressed to *ca.* 150° by admixture with the diazine from (II) (Found : N, 7·7. $C_{24}H_{20}O_4N_2$ requires N, 7·0%).

Attempted Decarboxylation of 2 : 3 : 4 : 6-*Tetramethoxyphenanthrene-9-carboxylic Acid*.—A mixture of the acid (0·2 g.) and freshly precipitated copper was slowly distilled in a high vacuum from an air bath at *ca.* 200°. The pinkish distillate was dissolved in ether, and the solution washed with dilute aqueous sodium hydroxide; the gum which remained after evaporation of the ether, when rubbed with methanol, gave crystals of methyl 2 : 3 : 4 : 6-tetramethoxyphenanthrene-9-carboxylate, m. p. and mixed m. p. 96—97°.

Deaminocolchinol Methyl Ether (XII).—This was prepared (*a*) as described by Windaus and Schiele (*Annalen*, 1924, **439**, 71) from the quaternary ammonium hydroxide obtained by exhaustive methylation of colchinol methyl ether; (*b*) by heating the corresponding carbonate alone at 250° or mixed with solid potassium hydroxide at 120°, followed by distillation in a high vacuum (air-bath at 140—150°); (*c*) as described in Part III, by the action of phosphoric oxide on *N*-acetylcolchinol methyl ether. In all of these cases the product, crystallised from methanol, melted finally within the range 111—113°, but in most cases there was a noticeable shrinking, and sometimes melting, followed by re-solidification, within the range 98—105°. A more intensive search in the crystallisation mother-liquors from (*c*), not attempted in the earlier experiments (*a*) and (*b*), yielded a few crystals, m. p. 99—100°, depressed to *ca.* 84° by the above compound, but not depressed by the *iso*deaminocolchinol methyl ether described below.

Deaminocolchinol methyl ether gave no intensification of colour or other evidence of picrate formation when added to a methanolic solution of picric acid. It was recovered unchanged (50 mg. from 60 mg.) after boiling for 3 hours with sodium methoxide (100 mg. of sodium in 2 c.c. of methanol). When it (50 mg.) was boiled for 2½ hours in acetic acid (1 c.c.) and hydrochloric acid (0·5 c.c.), a red-brown solution was obtained, from which, after dilution, washing its ethereal extract with dilute sodium hydroxide, and then distilling it in a high vacuum, a small amount of the original material was recovered, m. p. and mixed m. p. 109—110°, after softening at 101°.

Dehydration of the Carbinol formed by the Action of Nitrous Acid on Colchinol Methyl Ether.—This carbinol, prepared as described in Part I and purified through its *p*-phenylbenzoate, had m. p. 116° and $[\alpha]_{5461}^{17°}$ −138° (*c* = 2, in chloroform).

(*a*) A solution of the carbinol (600 mg.) in xylene (30 c.c.) was refluxed with phosphoric oxide (1·5 g.) for 10—15 minutes. The xylene solution was decanted, the residue extracted with hot xylene, and the solvent removed under reduced pressure from the combined solutions. The residual gum was distilled in a high vacuum from an air-bath at 145°, and gave a viscous distillate (230 mg.) and a non-volatile residue, which was not examined. The distillate, when rubbed with methanol, gave a solid, which was separated, by repeated crystallisation from methanol, into two main fractions : (i) a small quantity of deaminocolchinol methyl ether (XII), m. p. and mixed m. p. 109—111° (micro-hydrogenation with palladium-black gave 1·01 double bonds), and (ii) *isodeaminocolchinol methyl ether* (XIII), isolated in larger amount, m. p. 100—101°, depressed to 80—85° by admixture with (XII) (Found : C, 73·2; H, 6·3; double bond, by micro-hydrogenation with palladium-black, 0·93. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·4%). The presence of a third compound was established in the course of this fractional crystallisation. It was responsible for the cloudiness of the melts (*ca.* 100°) observed with several intermediate fractions, and eventually a few crystals, micro-m. p. 167—169°, were obtained, but the amount was insufficient for further examination.

(*b*) A mixture of the carbinol (200 mg.), m. p. 116°, and powdered potassium hydrogen sulphate (500 mg.) was heated for 1½ hours in an oil-bath at 170—180°, in a slow stream of dry carbon dioxide. The cooled mass was extracted with water and ether, leaving a small amount of white residue. This was soluble in benzene, but very sparingly soluble in methanol or *cyclo*hexane. Its mode of formation is uncertain, as the ether used for extraction was subsequently found to contain an appreciable amount of peroxide. This product, m. p. 205—207°, was not examined further. The resin obtained from the above ethereal extract was distilled in a vacuum. The distillate yielded a solid when rubbed and warmed with methanol, and fractional crystallisation gave deaminocolchinol methyl ether, m. p. and mixed m. p. 109—110°, as the chief constituent. The methanol mother-liquors deposited a second fraction from which, by recrystallisation, there was obtained a mixture in which individual crystals appeared to be the *iso*-compound (XIII) (micro-m. p. and mixed m. p. 91—95°), while other crystals (micro-m. p. 131—143°) appeared to contain the high-melting solid mentioned in the preceding paragraph.

9 : 12 : 13 : 14-*Tetramethoxy*-3 : 4 : 5 : 6-*dibenz*-$\Delta^{3:5}$-cyclo*heptadiene*.—(*a*) Deaminocolchinol methyl ether (XII) (150 mg.) was hydrogenated by means of palladium-black in acetic acid at room temperature and pressure, hydrogen

* Micro-melting points were determined by observing a crystal on an electrically heated microscope stage (H. Meyer, "Analyse und Konstitutionsermittlung organischer Verbindungen," Vienna, 1938, p. 86).

absorption (1·1 mols.) ceasing after an hour. The solvent was distilled under reduced pressure from the filtered solution; the residual *dihydride* crystallised in clusters of prisms (from methanol), m. p. 97° (Found: C, 72·7; H, 7·0. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·0%). (*b*) Micro-hydrogenation of *iso*deaminocolchinol methyl ether (XIII) under similar conditions gave the same dihydride, m. p. and mixed m. p. 96—97°.

The dihydride was recovered unchanged after being heated at 250—290° for 3 hours with palladium-black in a slow stream of carbon dioxide (under which conditions 9 : 10-dihydrophenanthrene gave phenanthrene in high yield) and also after being heated with selenium for 18 hours in open or evacuated sealed tubes at temperatures between 260° and 305°.

Oxidation of Deaminocolchinol Methyl Ether.—(a) *With sodium dichromate.* In view of the possibility that the compound was a fluorene derivative a quantity of oxidising agent insufficient for complete quinone formation was at first used. A solution of the compound (300 mg.) in acetic acid (0·6 c.c.) was treated with a solution of sodium dichromate (400 mg.) in water (0·15 c.c.) and acetic acid (0·5 c.c.), and the whole was heated at 100° for ½ hour. After dilution with water a chloroform extract of the mixture was washed with aqueous sodium carbonate and evaporated. The residual gum was warmed and rubbed with methanol, and the quinone, which crystallised in part, was collected. The mother-liquor was evaporated, and the residue dissolved in benzene–ligroin (1 : 3) and passed through a column of alumina, where separation occurred into a red upper band and a lower region of general adsorption. These were separately eluted, benzene alone ultimately being used as the solvent. The red eluate furnished some quinone, a further quantity being obtained from the yellow eluate after renewed oxidation and separation on alumina. The pale yellow gum which was the other product of this second chromatographic separation was worked up as described below. The combined quinone fraction crystallised from acetic acid in the two forms, m. p. 193°, and did not depress the m. p. of synthetic 2 : 3 : 4 : 7-tetramethoxyphenanthraquinone (II). The corresponding diazines also were identical, m. p. and mixed m. p. 175—176°, rising to 185° on remelting.

The aforesaid pale yellow gum set to a glass on standing. When warmed and rubbed with methanol, this yielded a small amount of a solid, which, after several recrystallisations from methanol, formed cream-coloured needles, m. p. 109—111° (Found: C, 69·45; H, 5·5. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·5%). This compound was probably 9 : 12 : 13 : 14-*tetramethoxy*-3 : 4 : 5 : 6-*dibenz*-$\Delta^{1:8:5}$-cyclo*heptatrien*-7-*one*, but because of the small quantity available no derivative was prepared. It was insoluble in alkali, gave an immediate red precipitate with 2 : 4-dinitrophenylhydrazine in ethanol–sulphuric acid, and dissolved in concentrated hydrochloric acid to an orange-red solution.

(b) *With osmium tetroxide.* A solution of deaminocolchinol methyl ether (100 mg.) in dry ether (5 c.c.) was treated with osmium tetroxide (90 mg.) in ether (5 c.c.). After 4 days, the ether was evaporated, and the residual black powder heated under reflux for 2½ hours with a solution of hydrated sodium sulphite (0·9 g.) in water (10 c.c.) and methanol (20 c.c.). Undissolved solid was collected, extracted twice with boiling methanol, and the combined filtrate and extract boiled with charcoal and evaporated under reduced pressure. The residue was treated with water, and the suspension extracted with ether. Evaporation of the ether gave cis-1 : 2-*dihydroxy*-9 : 12 : 13 : 14-*tetramethoxy*-3 : 4 : 5 : 6-*dibenz*-$\Delta^{3:8}$-cyclo*heptadiene* as colourless slender rods (from aqueous methanol), m. p. 165—166° (Found: C, 66·0; H, 5·9. $C_{19}H_{22}O_6$ requires C, 65·9; H, 6·4%).

2 : 3 : 4 : 7-*Tetramethoxy*-10-*phenanthraldehyde* (XI).—Lead tetra-acetate (80 mg.) was added portionwise, with shaking and exclusion of moisture, to a solution of the aforesaid *cis*-glycol (60 mg.) in dry benzene (12 c.c.), maintained at 40°. The mixture was heated to boiling and then set aside for an hour at room temperature. After filtration, the benzene solution was washed with water, dried, and evaporated. A solution of the resulting gum in methanol very slowly deposited (2 days) a few crystals of the *aldehyde* (XI), but subsequent experience showed that addition of a trace of sodium carbonate to the warm solution caused immediate crystallisation of the aldehyde (73% yield). It formed a mass of bright yellow needles, m. p. 130—131°, depressed to 100—110° by admixture with 2 : 3 : 4 : 7-tetramethoxy-9-phenanthraldehyde (Found: C, 69·7; H, 5·9. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·5%), and gave an *oxime*, m. p. 169—170°, depressed to *ca.* 140° by admixture with the oxime of the 9-aldehyde (below) (Found: C, 66·8; H, 5·3; N, 4·6. $C_{19}H_{19}O_5N$ requires C, 66·85; H, 5·6; N, 4·1%).

A solution of the aldehyde (XI) (18 mg.) in purified acetone (1 c.c.) was oxidised at 50—60° by addition of a 6% solution of potassium permanganate in acetone (0·1 c.c.). After the mixture had been kept overnight at room temperature, sulphurous acid was added, and the whole extracted with chloroform. The acidic product was separated from unchanged aldehyde (12 mg. recovered) by extraction with sodium carbonate solution; the precipitated acid formed pale yellow needles (from dilute ethanol), micro-m. p. 198—201°, not depressed by admixture with a synthetic specimen of 2 : 3 : 4 : 7-tetramethoxyphenanthrene-10-carboxylic acid (I). Ethereal diazomethane gave the corresponding methyl ester, micro-m. p. and mixed m. p. 101—103°.

Action of Nitrosyl Chloride on Deaminocolchinol Methyl Ether.—Attempts were made to effect addition of nitrosyl chloride to the double bond, with a view to subsequent elimination of hydrogen chloride and production of the oxime of the corresponding unsaturated ketone. When deaminocolchinol methyl ether was treated with amyl nitrite and hydrogen chloride in acetic acid at −15°, it did not react and was recovered. Reaction took place by addition of excess of a solution of nitrosyl chloride in ether to an ethereal solution of the unsaturated compound at −15° to −20°. The crystalline *product* separated from methanol as a yellow powder, micro-m. p. 136—143° (Found: C, 52·9; H, 4·4%). This substance was heated with pyridine on the water-bath, and the product distilled from a bath at 180—210°/0·2 mm. The resulting yellow prisms had m. p. 174—175° (from methanol). It was evident from the analytical figures that nitrosyl chloride had effected chlorination in addition to possible addition to the double bond, and the *compound* obtained with pyridine was not further investigated (Found: C, 58·9; H, 5·1; N, 3·9; Cl, 9·6%).

Oxidation of iso*Deaminocolchinol Methyl Ether.*—A slightly impure specimen of the *iso*-compound (XIII) (34 mg.), m. p. 93—99°, was oxidised as described above, with osmium tetroxide in ether. The crude product was crystallised from methanol and a crystal examined had micro-m. p. 162—168°, depressed to 140—160° by admixture with the diol formed from (XII). The crystallised product, together with that recovered from the mother-liquor, was oxidised with lead tetra-acetate in the manner described. The resulting gummy aldehyde crystallised from methanol in presence of a trace of sodium carbonate, and had micro-m. p. 129—133°, raised to 130—134° by admixture with 2 : 3 : 4 : 7-tetramethoxy-9-phenanthraldehyde (aldehyde-A of Part IV), and depressed to 112—116° by admixture with the 10-aldehyde (XI). It gave an *oxime*, micro-m. p. 166—169°, not depressed by a specimen, m. p. 169—170°, prepared from the synthetic 9-aldehyde (Found: C, 67·1; H, 5·3; N, 4·5. $C_{19}H_{19}O_5N$ requires C, 66·85; H, 5·6; N, 4·1%).

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45. *Anthraquinone Series. Part I. 2-Alkylanthraquinones.*

By A. T. Peters and F. M. Rowe.

2-*tert.*-Butyl- and 2-*n*-butyl-anthraquinone are prepared in 75% and 72% yield, respectively, by direct cyclisation of the corresponding 2-(4'-butylbenzoyl)benzoic acid with 20% fuming sulphuric acid at 95° and 100°, respectively. 2-*iso*Propylanthraquinone is obtained similarly in 33% yield, but the method of ring closure is not applicable to the higher alkyl analogues, *viz.*, *n*-amyl, *n*-heptyl, *n*-octyl, and *n*-dodecyl. 2-*tert.*-Butylanthraquinone is also prepared by cyclisation of 2-(4'-tert.-*butylbenzyl*)*benzoic acid* to 2-tert.-*butyl*-9-*anthrone* with 100% sulphuric acid at 50°, followed by oxidation with chromic acid.

This investigation began with an attempt to prepare 2-*tert.*-butylanthraquinone (I) readily. The sole previous reference to (I) is by Backer and Strating (*Rec. Trav. chim.*, 1934, **53**, 525), who prepared it from *tert.*-butylbutadiene and α-naphthaquinone, followed by air oxidation of the resulting 2-*tert.*-butyl-1 : 4 : 11 : 12-tetrahydroanthraquinone. We have prepared (I) in 75% yield by direct cyclisation of 2-(4'-tert.-*butylbenzoyl*)-*benzoic acid* (II) with 20% fuming sulphuric acid at 95°, the product being almost pure. Such a facile cyclisation was unexpected, as Scholl and co-workers (*Monatsh.*, 1911, **32**, 687) stated that satisfactory ring closure of 2-(4'-alkylbenzoyl)benzoic acids with sulphuric acid was impracticable where alkyl is higher than methyl because of simultaneous sulphonation. Prolonged reduction (Clemmensen) of (II) afforded 2-(4'-tert.-*butylbenzyl*)*benzoic acid* (III), whereas the use of zinc and aqueous-alcoholic sodium hydroxide yielded the *lactone* of 2-*carboxy*-4'-tert.-*butyldiphenylcarbinol*. (III) was readily cyclised by 100% sulphuric acid at 50° to 2-tert.-*butyl*-9-*anthrone*, which was oxidised by chromic acid in acetic acid to (I). Such a method of oxidation is not applicable to all alkylanthrones, but in the above case, the stability of the *tert.*-butyl group allows an almost quantitative conversion into (I); a similar stability of *tert.*-butyl was observed with 2-*tert.*-butylnaphthalene (Bromby, Peters, and Rowe, J., 1943, 144) and 3-*tert.*-butylacenaphthene (Peters, J., 1942, 562).

In view of the ready cyclisation of (II), it was of interest to determine how general was this method for preparing 2-alkylanthraquinones. 2-*iso*Propylanthraquinone was obtained similarly in only 33% yield, as sulphonation accompanied cyclisation, but 2-(4'-*n*-butylbenzoyl)benzoic acid was converted by 20% or 25% fuming sulphuric acid at 100° into 2-*n*-butylanthraquinone in 72% yield, a method of preparation far superior to that of Harris *et al.* (J., 1936, 1838) *via* the benzylbenzoic acid and the anthrone. Attempts to extend the method to higher alkyl analogues, however, failed. 2-*n*-Dodecylanthraquinone could not be prepared similarly from 2-(4'-n-*dodecylbenzoyl*)*benzoic acid*, water-soluble products only being obtained with various strengths of sulphuric acid at 0° to 120°; moreover, attempts at cyclisation also failed using fuming sulphuric acid and boric acid, chlorosulphonic acid, aluminium chloride, phosphorus pentachloride and pentoxide, and zinc chloride. In order to determine the limit of applicability of the direct cyclisation method, 2-(4'-n-*octylbenzoyl*)*benzoic acid*, the *n*-heptyl analogue, and 2-(4'-n-*amylbenzoyl*)*benzoic acid* were prepared by the Friedel–Crafts reaction, but all behaved similarly to the *n*-dodecyl analogue on attempted cyclisation with sulphuric acid under a variety of conditions.

Experimental.

2-(4'-tert.-*Butylbenzoyl*)*benzoic Acid* (II).—*tert.*-Butylbenzene (50 g.; 1 mol.) (Bromby *et al.*, *loc. cit.*) in carbon disulphide (120 c.c.) was added to phthalic anhydride (60 g.; 1·08 mols.) and aluminium chloride (110 g.; 2·2 mols.), and after refluxing for 6 hours on the water-bath, solvent was removed, and the residue warmed with dilute hydrochloric acid. The sticky solid was collected and extracted with warm 15% aqueous sodium carbonate, the alkaline solution acidified, and the sticky precipitate kept at 0° for 24 hours; it then solidified. It was dissolved in ether, and solvent removed from the dried (Na_2SO_4) extract; the residue crystallised from benzene–light petroleum (1 : 4) in colourless, prismatic needles, m. p. 148—149°, of the *acid* (II) (yield, 69 g.; 65·6%) (Found: C, 76·6; H, 6·3. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%). It separated from aqueous solvents in resinous form. Like other alkyl analogues, it is a powerful nose irritant.

2-tert.-*Butylanthraquinone* (I).—The above carboxylic acid (20 g.) was heated with 20% fuming sulphuric acid (100 g.) at 95° for 1·5 hours, the mixture poured on ice (500 g.), and the precipitate extracted with boiling 15% aqueous sodium carbonate. The residue (I), m. p. 98° (yield, 14 g.; 74·8%), crystallised from methyl alcohol in pale yellow needles, m. p. 104° (Found: C, 82·1; H, 5·9. Calc. for $C_{18}H_{16}O_2$: C, 81·8; H, 6·0%). Unchanged acid (II) (2 g.) was recoverable from the sodium carbonate extracts. Addition of boric anhydride to the reaction mixture did not influence the yield of (I), and concentrated sulphuric acid at 135—140° gave a yield of only 30%; 25% fuming sulphuric acid at 94—95°, however, afforded a 70% conversion of (II) into (I).

Lactone of 2-*Carboxy*-4-tert.-*butyldiphenylcarbinol*.—2-(4'-*tert.*-Butylbenzoyl)benzoic acid (10 g.) was refluxed with 6N-sodium hydroxide (70 c.c.), alcohol (120 c.c.), and zinc dust (50 g.), or with 2N-sodium hydroxide (250 c.c.), zinc dust (30 g.), and 40 c.c. of a solution prepared from equal volumes of 2N-aqueous ammonia and 2N-copper sulphate, for 30 hours (cf. Scholl and Neovius, *Ber.*, 1911, **44**, 1077). The *lactone* crystallised from alcohol in colourless needles, m. p. 125—126° (yield, 5·8 g. or 6·1 g.; 61·5 or 64·7%, respectively) (Found: C, 80·7; H, 6·9. $C_{18}H_{16}O_2$ requires C, 81·2; H, 6·8%), insoluble in aqueous alkalis.

2-(4'-tert.-*Butylbenzyl*)*benzoic Acid* (III).—2-(4'-*tert.*-Butylbenzoyl)benzoic acid (20 g.) was refluxed with amalgamated zinc (from 60 g. of zinc) and concentrated hydrochloric acid (250 c.c.). After 10 hours, much of the above lactone was present, but after refluxing for 50 hours and cooling, a transparent sticky glass was obtained. It was extracted with boiling 15% aqueous sodium carbonate, and the alkaline extract acidified at 0°. After solution of the sticky precipitate several times in aqueous sodium carbonate and precipitation with dilute acid, the product was dissolved in ether, solvent removed, and the residue kept at 0° for 48 hours. It was crystallised several times from light petroleum, from which the *acid* separated in colourless, prismatic needles, m. p. 108—110° (yield, 5·1 g.; 53·7%) (Found: C, 80·1; H, 7·4. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·4%), readily soluble in aqueous alkalis.

2-tert.-*Butyl*-9-*anthrone*.—2-(4'-*tert.*-Butylbenzyl)benzoic acid (4 g.) was warmed with 100% sulphuric acid (20 g.) at 50° for 30 minutes. After addition to ice, the precipitate was extracted with boiling 15% aqueous sodium carbonate, and the insoluble residue crystallised from light petroleum. The *anthrone* separated in long, colourless, prismatic needles,

m. p. 117—118° (yield, 2·7 g.; 67·5%) (Found: C, 85·8; H, 7·2. $C_{18}H_{16}O$ requires C, 86·4; H, 7·2%). It crystallised unchanged from acetic anhydride, and afforded a green vat dye with chloranil.

Oxidation of 2-tert.-*Butyl*-9-*anthrone*.—A much more convenient method than those employed for analogous oxidations, *viz.*, bromine in acetic acid (Scholl *et al.*, *loc. cit.*) or hydrolysis of the derived *p*-nitrosodimethylanil (Harris *et al.*, *loc. cit.*), was used. The anthrone (2·5 g.) was readily converted into (I) (yield, 2·5 g.; 95%) by boiling with chromic acid (4 g.) in acetic acid (25 c.c.) for 10 minutes.

n-*Butylbenzene* (cf. Harris *et al.*, *loc. cit.*).—*n*-Butyl bromide (117 g.; 1·15 mols.), bromobenzene (117 g.; 1 mol.), and sliced sodium (70 g.; 4 atoms) in dry benzene (200 c.c.) were allowed to react in a 3 l. flask without external heat, and after the vigorous reaction had subsided, the mixture was refluxed for 4 hours and left overnight at room temperature. Benzene was removed, and the residue fractionated. *n*-Butylbenzene distilled as a colourless oil, b. p. 183—186° (yield, 38 g.; 38%) (Harris *et al.* gave no details of preparation and recorded 28% yield). It is best not to use *n*-butyl bromide in too large excess.

2-(4′-n-*Butylbenzoyl*)*benzoic Acid* (cf. Underwood and Walsh, *J. Amer. Chem. Soc.*, 1935, **57**, 940; Harris *et al.*, *loc. cit.*).—*n*-Butylbenzene (50 g.; 1 mol.) was added to phthalic anhydride (60 g.; 1·08 mols.) and aluminium chloride (110 g.; 2·2 mols.) in carbon disulphide (160 c.c.), and after refluxing for 7 hours, the mixture was treated in similar manner to that described for the *tert.*-butyl analogue. The acid crystallised from benzene–light petroleum (1 : 5) in colourless, prismatic needles, m. p. 99—100° (yield, 70 g.; 67%).

2-n-*Butylanthraquinone*.—The above acid (5 g.) was heated with 20% or 25% fuming sulphuric acid (20 g.) in a boiling water-bath for 1·5 hours, the product added to ice, and the precipitate extracted with boiling 15% aqueous sodium carbonate; the residue was a pale yellow solid, m. p. 86—87°. Crystallisation from light petroleum gave pale cream, prismatic needles, m. p. 90°, of 2-*n*-butylanthraquinone (yield, 3·4 g.; 72%) (Found: C, 81·8; H, 6·0. Calc. for $C_{18}H_{16}O_2$: C, 81·8; H, 6·0%) [Harris *et al.*, *loc. cit.*, described the compound as a green powder, m. p. 72°, which after two crystallisations from alcohol had m. p. 87·5°, and they obtained only 56% conversion of 2-(4′-*n*-butylbenzyl)benzoic acid into crude 2-*n*-butyl-9-anthrone]. Other conditions for cyclisation of 2-(4′-*n*-butylbenzoyl)benzoic acid (5 g.) by 25% fuming sulphuric acid (20 g.), with yields of 2-*n*-butylanthraquinone in parentheses, are: room temperature for 2 days (1·25 g.; 27%); 120° for 1 hr. (mainly charred product); 80—85° for 1·5 hours (2·8 g.; 60%); 95° for 1 or 2 hours (3·3 or 3·2 g.; 70 or 68%, respectively); in presence of boric anhydride (5 g.) at 95° for 1 hour (2·8 g.; 60%).

2-(4′-iso*Propylbenzoyl*)*benzoic Acid*.—*iso*Propylbenzene (12 g.; 1 mol.), phthalic anhydride (16 g.; 1·1 mols.), and aluminium chloride (30 g.; 2·2 mols.) in carbon disulphide (120 c.c.), refluxed for 7 hours, gave the acid, which crystallised from light petroleum in colourless prisms, m. p. 129—130° (yield, 21 g.; 78·3%) (Scholl *et al.*, *loc. cit.*, gave m. p. 134°).

2-iso*Propylanthraquinone*.—The above acid (2 g.) and 20% fuming sulphuric acid (10 g.) at 95° for 1 hour gave 2-*iso*propylanthraquinone, which crystallised from light petroleum in pale yellow prisms, m. p. 45° (yield, 0·63 g.; 33%).

n-*Dodecylbenzene*.—*n*-Dodecyl bromide (25 g.; 1 mol.), bromobenzene 17 g.; 1·1 mols.), and sodium (6·9 g.; 3 atoms) in dry benzene (60 c.c.) were refluxed for 5 hours, and the product fractionated. *n*-Dodecylbenzene distilled as a colourless oil, b. p. 172—174°/6 mm. (yield, 10·3 g.; 40%).

2-(4′-n-*Dodecylbenzoyl*)*benzoic Acid*.—*n*-Dodecylbenzene (25 g.; 1 mol.), phthalic anhydride (16·5 g.; 1·1 mols.), and aluminium chloride (29 g.; 2·2 mols.) in carbon disulphide (150 c.c.), refluxed for 12 hours, gave the *acid*, which crystallised from light petroleum in colourless needles, m. p. 96—97° (yield, 18·1 g.; 43·3%) (Found: C, 79·0; H, 8·8. $C_{26}H_{34}O_3$ requires C, 79·2; H, 8·6%).

n-*Octylbenzene* (cf. Schweinitz, *Ber.*, 1886, **19**, 640; Ahrens, *ibid.*, p. 2717).—*n*-Octyl bromide (31 g.; 1·05 mols.), bromobenzene (24 g.; 1 mol.), and sodium (11 g.; 3·1 atoms) in dry ether (100 c.c.), refluxed for 7 hours, gave *n*-octylbenzene, b. p. 262—264°/759 mm. (yield, 12·8 g.; 44%).

2-(4′-n-*Octylbenzoyl*)*benzoic Acid*.—*n*-Octylbenzene (3·6 g.; 1 mol.), phthalic anhydride (3 g.; 1·08 mols.), and aluminium chloride (5·7 g.; 2·2 mols.) in carbon disulphide (60 c.c.), refluxed for 6 hours, gave the *acid*, which separated from light petroleum in colourless needles, m. p. 80° (yield, 2·5 g.; 41%) (Found: C, 78·3; H, 7·8. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%).

n-*Heptylbenzene* (cf. Harris *et al.*, *loc. cit.*).—*n*-Heptyl bromide (25 g.; 1 mol.), bromobenzene (23 g.; 1·1 mols.), and sodium (12 g.; 4 atoms) in ether (80 c.c.), refluxed for 6 hours, gave *n*-heptylbenzene, b. p. 241—242°/761 mm. (yield, 10·6 g.; 43·3%).

2-(4′-n-*Heptylbenzoyl*)*benzoic Acid*.—*n*-Heptylbenzene (8·8 g.; 1 mol.), phthalic anhydride (8 g.; 1·08 mols.), and aluminium chloride (15 g.; 2·2 mols.) in carbon disulphide (80 c.c.), refluxed for 6 hours, gave the acid, which crystallised from light petroleum in colourless needles, m. p. 103° (yield, 11·5 g.; 71%) (Harris *et al.* recorded pale yellow crystals, m. p. 99—101°).

n-*Amylbenzene* (cf. Schramm, *Annalen*, 1883, **218**, 388).—*n*-Butyl bromide (16·4 g.; 1·2 mols.), benzyl bromide (17·1 g.; 1 mol.), and sodium (6·9 g.; 3 atoms) in ether (100 c.c.), refluxed for 8 hours, gave *n*-amylbenzene, b. p. 200—202°/759 mm. (yield, 4·1 g.; 28%).

2-(4′-*Amylbenzoyl*)*benzoic Acid*.—*n*-Amylbenzene (3 g.; 1 mol.), phthalic anhydride (3·2 g.; 1·08 mols.), and aluminium chloride (5·8 g.; 2·2 mols.) in carbon disulphide (60 c.c.), refluxed for 7 hours, gave the *acid*, which crystallised from light petroleum in minute, colourless needles, m. p. 99—100° (yield, 2·4 g.; 40%) (m. p. of *n*-butyl analogue is depressed to 90—91°) (Found: C, 77·0; H, 6·6. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%).

Attempted Cyclisation of 2-(4′-n-*Alkylbenzoyl*)*benzoic Acids*.—In the cases of the acid where alkyl is *n*-dodecyl, *n*-octyl, *n*-heptyl, or *n*-amyl, in contrast to those instances where alkyl is *iso*propyl or *n*- or *tert.*-butyl, the following agents failed to effect cyclisation, giving mainly water-soluble products: concentrated or 100% sulphuric acid; 5%, 10%, 20%, 25%, or 65% fuming sulphuric acid, with or without boric acid or boric anhydride, at 0° to 120°, for various time periods.

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46. *Sulphonamides derived from Substituted Anilines.*

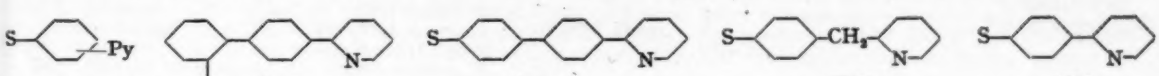
By A. H. Cook, I. M. Heilbron, and K. J. Reed.

A variety of sulphanilamidophenyl-pyridines, -phenylpyridines, -lutidines, -thiazoles, and one sulphanilamidophenylpyrimidine have been synthesised, usually from the appropriate substituted aniline. Many of these sulphonamides showed considerable antibacterial action *in vitro*, though *in vivo* tests revealed disadvantages.

AMONG the most successful of the sulphonamide drugs have been those with the sulphanilamido-group attached directly to a heterocyclic system as in sulphapyridine. There have been many attempts to improve the action of these drugs, *e.g.*, by inserting a single methylene group between the sulphanilamido-system and the heterocyclic ring, by using polynuclear ring-systems such as quinolyl or acridyl, or by preparing sulphanilamidobenzene derivatives.

Recent work in these laboratories (see, *e.g.*, Heilbron, Hey, and Lambert, J., 1940, 1279) had provided a variety of pyridylanilines of known orientation and it seemed worth while to prepare the corresponding sulphanilamides by interaction with acetylsulphanilyl chloride and removal of the acetyl group in the usual manner. The resulting *compounds* (I) thus resembled sulphapyridine except that a benzene ring was inserted between the sulphanilamido- and the pyridyl group.

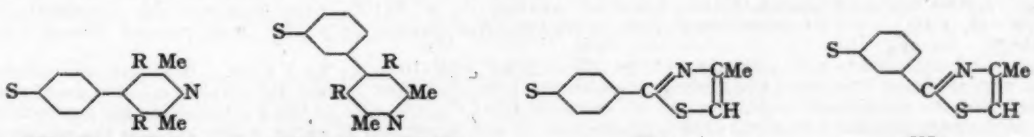
Promising *in vitro* and *in vivo* tests suggested that the anti-bacterial effect might remain when two benzene rings were inserted between the sulphanilamide and the pyridyl residue, or when the pyridyl ring in compounds (I) was replaced by the thiazole ring. Accordingly 2-amino- and 4-amino-4′-α-pyridyldiphenyl were converted into *sulphonamides* (II) and (III) respectively. The acetyl derivatives of these compounds were almost insoluble in dilute acid or alkali and, although the anticipated sulphonamide nature was confirmed, they were of no obvious practical value; attention was therefore redirected to those sulphonamides with only one ring separating the sulphanilamide and the heterocyclic group. It is interesting that (IV), prepared from α-4-aminobenzylpyridine, had considerable potency compared with α-4-*sulphanilamidophenylpyridine* (V). Compounds (VI)—(IX) were prepared in the normal manner from the appropriate amines. (VIII) was also



(I.) (II.) (III.) (IV.) (V.)

(S = *p*-NH_2·C_6H_4·SO_2·NH)

prepared from the requisite amine and *p*-nitrobenzenesulphonyl chloride, followed by reduction. 2-Phenyl-4-methylthiazole had previously been nitrated (Friedman, Sparks, and Adam, *J. Amer. Chem. Soc.*, 1937, **59**, 2262) to a mononitro-compound. Thiobenzamide, obtained in excellent yield by refluxing benzonitrile with alcoholic ammonium sulphide, was converted into the thiazole, but repetition of these workers' nitration procedure gave a mixture. After separation, one component was shown to be the 4′-*nitro*-compound by oxidation to *p*-nitrobenzoic acid, and since it yielded the second component on further nitration, the latter must be formulated as 2′ : 4′-*dinitrophenyl*-4-*methylthiazole*. In consequence of these difficulties in the preparation of 2-*p*-aminophenyl-4-methylthiazole *p*-acetamidothiobenzamide was condensed with bromoacetone, and 2-p-*acetamidophenyl*-4-*methylthiazole* hydrolysed to the required base. The corresponding sulphonamide (X) was



(VI.) R = CO_2Et (VII.) R = H (VIII.) R = CO_2Et (IX.) R = H (X.) (XI.)

prepared in the normal manner, and in similar fashion the isomeric sulphonamide (XI) also was obtained. Attempts were then made to synthesise 2-*o*-aminophenyl-4-methylthiazole by similar steps. However, *o*-acetamidobenzonitrile on heating with ethanolamine and alcoholic hydrogen sulphide afforded mainly 2-methyl-4-thioquinazolone (cf. Bogert, Brenemann, and Hand, *J. Amer. Chem. Soc.*, 1903, **25**, 376) and only a very small yield of the required o-*acetamidothiobenzamide*. Moreover, acetylation of *o*-aminobenzonitrile yielded some 2-methylquinazolone in addition to the normal acetyl compound. This undesired cyclisation was prevented by working with o-*acetylsulphanilamidobenzonitrile*; this was converted into o-*acetylsulphanilamidothiobenzamide*, and the latter condensed with bromoacetone to give 2-o-*acetylsulphanilamidophenyl*-4-*methylthiazole*, hydrolysis of which gave the required *sulphonamide* directly.

2-Phenyl-4 : 6-dimethylpyrimidine had been previously nitrated by Ochiai *et al.* (*J. Pharm. Soc. Japan*, 1939, **59**, 462), though it appears that the constitution of the mononitro-product was not ascertained. We had no difficulty in obtaining the same compound, but as it was oxidised to *m*-nitrobenzoic acid, it must be unexpectedly formulated as the *m*-nitro-compound. It was converted by the ordinary reactions into 2-m-*sulphanilamidophenyl*-4 : 6-*dimethylpyrimidine*.

The antibacterial potency of most of the above compounds was compared with that of sulphapyridine in the Department of Experimental Medicine, Glaxo Laboratories Ltd., under the direction of Dr. J. Ungar, to whom our thanks are due. They were tested in synthetic medium and in most cases in 1% glucose and in 10% serum broth against several organisms. The results are in the table. *In vivo* tests (mice infected with *Streptococcus* or *Pneumococcus* and the drugs administered orally, by intraperitoneal or rarely intramuscular injection) showed some of these compounds to be probably less toxic than sulphapyridine, though they were either less effective or had disadvantageous solubilities.

Compound.	Solubility in synthetic medium.	Inhibition in synthetic medium.	Inhibition in glucose broth.
α-2-Sulphanilamidophenylpyridine	Insol. 1/10,000	Nil	Nil
β-2-Sulphanilamidophenylpyridine *	Insol. 1/50,000	*B. subtilis* 1/100,000	Nil
α-3-Sulphanilamidophenylpyridine *	Insol. 1/10,000	*Staph.* 1/5000 *Strep.* 1/500,000 *B. subtilis* 1/100,000	*Strep.* 1/5000 *Pneumo.* 1/50,000
α-4-Sulphanilamidophenylpyridine	Sol. 1/10,000	*B. coli* 1/5000 *Strep.* 1/10,000 *B. subtilis*, slight	*Strep.* 1/5000 *Pneumo.* 1/50,000
γ-4-Sulphanilamidophenylpyridine	Insol. 1/5000	*Strep.* 1/200,000 *B. subtilis* 1/100,000	*Strep.* 1/5000
α-4-Sulphanilamidobenzylpyridine *	Insol. 1/50,000	*Strep.* 1/50,000 *B. subtilis* 1/500,000	*Pneumo.* 1/100,000
2-(*o*-Sulphanilamidophenyl)-4-methylthiazole	Insol. 1/50,000	*B. subtilis* 1/500,000	Nil
2-(*m*-Sulphanilamidophenyl)-4-methylthiazole	Insol. 1/10,000	*Staph.* 1/1000	Nil
2-(*p*-Sulphanilamidophenyl)-4-methylthiazole	Insol. 1/10,000	*Strep.* 1/500,000 *B. subtilis* 1/100,000	*Strep.* 1/10,000 *Pneumo.* slight
3 : 5-Dicarbethoxy-4-(*m*-sulphanilamidophenyl)-2 : 6-lutidine	Insol. 1/10,000	Nil	Not tried
4-(*m*-Sulphanilamidophenyl)-2 : 6-lutidine	Insol. 1/10,000	*Staph.* 1/1000	Not tried
3 : 5-Dicarbethoxy-4-(*p*-sulphanilamidophenyl)-2 : 6-lutidine	Insol. 1/50,000	*Staph.*, *Strep.* *B. subtilis*, *coli*, slight inhib.	Nil Nil
2-(*p*-Sulphanilamidophenyl)-4 : 6-dimethylpyrimidine	Insol. 1/10,000	*Staph.* 1/5000 *B. coli* 1/1000	Not tried
Sulphapyridine *	Insol. 1/5000	*Pneumo.* 1/10,000 *Strep.* 1/100,000 *B. subtilis* 1/10⁶	Nil

* In these cases, the effects of *p*-aminobenzoic acid was examined. The effect of the sulphonamides (1/1000) on *B. subtilis* was completely neutralised by the natural vitamin (1/5000).

Experimental.

Sulphanilamidophenylpyridines.—α-2-, β-2-, α-3-, α-4-, and γ-4-Aminophenylpyridines were obtained by the methods of Heilbron, Hey, and co-workers (J., 1940, 349, 355). α-3-Aminophenylpyridine, previously described as an oil, was obtained as a solid crystallising in rhombs, m. p. 72—74°, from light petroleum (Found: C, 78·1, 77·7; H, 6·0, 6·05. Calc. for $C_{11}H_{10}N_2$: C, 77·8; H, 5·9%). The amines were dissolved or suspended in pyridine (*ca.* 6 mols.) and treated slowly with *N*-acetylsulphanilyl chloride (1 mol.) in the cold. The mixtures were heated at 100° for 1 hour, and the acetylsulphanilyl compounds precipitated with water and allowed to crystallise; they were freely soluble in dilute sodium hydroxide solution. The following were prepared: α-2-N⁴-*Acetylsulphanilamidophenylpyridine*, small prismatic needles, m. p. 150—151°, from ethanol (Found: C, 62·1; H, 4·5. $C_{19}H_{17}O_3N_3S$ requires C, 62·1; H, 4·6%). β-2-N⁴-*Acetylsulphanilamidophenylpyridine*, needles, m. p. 168·5—169°, from dilute ethanol (Found: C, 62·05; H, 4·9%). α-3-N⁴-*Acetylsulphanilamidophenylpyridine*, pale yellow needles, m. p. 223—225°, from ethanol (Found: C, 62·4; H, 4·85%). α-4-N⁴-*Acetylsulphanilamidophenylpyridine*, needles, m. p. 241·5°, from acetone–light petroleum (Found: C, 62·25; H, 4·8%). γ-4-N⁴-*Acetylsulphanilamidophenylpyridine*, prisms, m. p. 272°, from ethanol (Found: C, 61·9; H, 4·85%).

The acetyl compounds were refluxed with 2N-hydrochloric acid (10 vols.) for 1 hour. The clear cold solution was treated with sufficient 2N-sodium hydroxide to dissolve the precipitate first formed, the alkaline solution decolorised with charcoal, and the sulphonamide precipitated by neutralisation. In the case of the 4-γ-isomeride the hydrochloride of the sulphonamide separated from the cold acid solution; it was suspended in water, converted into the soluble sodium salt, decolorised and precipitated as usual. With the preceding exception the sulphonamides were freely soluble in dilute acid or alkali and gave azo-dyes on diazotisation and coupling. The following were prepared: α-2-*Sulphanilamidophenylpyridine*, pale yellow prisms, m. p. 200°, from acetone–water (Found: C, 62·9; H, 4·5. $C_{17}H_{15}O_2N_3S$ requires C, 62·7; H, 4·6%). β-2-*Sulphanilamidophenylpyridine*, prisms, m. p. 186—186·5°, from dilute ethanol (Found: C, 62·8; H, 4·8%). α-3-*Sulphanilamidophenylpyridine*, plates, m. p. 170°, from dilute ethanol (Found: C, 62·9; H, 4·85%). α-4-*Sulphanilamidophenylpyridine*, needles, m. p. 257·5°, from ethanol (Found: C, 62·5; H, 5·0%). γ-4-*Sulphanilamidophenylpyridine*, pale yellow needles, m. p. 217—218°, from ethanol–water (Found: C, 62·9; H, 4·6%).

α-4-Aminobenzylpyridine (Tschitschibabin, Kuindishi, and Benewolenskara, *Ber.*, 1925, **58**, 1583) (9 g.) in pyridine (25 c.c.) was treated with acetylsulphanilyl chloride (12 g.); after 12 hours, addition of water precipitated α-4-N⁴-*acetylsulphanilamidobenzylpyridine* (17·8 g.); it crystallised in needles, m. p. 217—219°, from dilute ethanol (Found: C, 63·35; H, 5·0. $C_{20}H_{19}O_3N_3S$ requires C, 63·0; H, 5·0%). Hydrolysis with 2N-hydrochloric acid (10 vols.) for 30 mins. in the normal manner afforded α-4-*sulphanilamidobenzylpyridine* (14·5 g.). It formed prismatic needles, m. p. 154°, from dilute ethanol (Found: C, 63·8; H, 4·9. $C_{18}H_{17}O_2N_3S$ requires C, 63·7; H, 5·0%).

Sulphanilamidopyridyldiphenyls.—The *N*⁴-acetyl compounds were prepared in excellent yields from the aminopyridyldiphenyls (Heilbron, Hey, and Lambert, *loc. cit.*) as with the aminophenylpyridines above. 2′-N⁴-*Acetylsulphanilamido*-4-α-*pyridyldiphenyl* formed needles, m. p. 193—194°, from acetone–light petroleum. 4′-N⁴-*Acetylsulphanilamido*-4-α-*pyridyldiphenyl* separated from ethanol in needles, m. p. 275—277° (Found: C, 67·3; H, 4·95. $C_{25}H_{21}O_3N_3S$ requires C, 67·7; H, 4·75%). Hydrolysis of the acetyl compounds was effected by boiling with dilute hydrochloric acid for ½—1 hr. and neutralising the solution. 2′-*Sulphanilamido*-4-α-*pyridyldiphenyl* crystallised from dilute ethanol in small plates, m. p. 164—165° (Found: C, 69·2; H, 4·9. $C_{23}H_{19}O_2N_3S$ requires C, 68·8; H, 4·75%); 4′-*sulphanilamido*-4-α-*pyridyldiphenyl*, crystallised from acetic acid, had m. p. 298—299° (Found: C, 68·6; H, 4·8. $C_{23}H_{19}O_2N_3S$ requires C, 68·8; H, 4·75%).

Sulphanilamidophenyl-lutidines.—Acetylsulphanilyl chloride (1·22 g.) was warmed for 1 hr. at 100° with ethyl 4-*p*-aminophenyl-2 : 6-dimethylpyridine-3 : 5-dicarboxylate (Cook, Heilbron, and Steger, J., 1943, 413) (1·7 g.) and pyridine (10 c.c.), and the product (2·6 g., m. p. 242—243°) precipitated with water (50 c.c.); the N⁴-*acetylsulphanilyl* derivative separated from dilute ethanol in prismatic needles, m. p. 243—244° (Found: C, 60·4; H, 5·35. $C_{31}H_{32}O_7N_3S$ requires C, 60·1; H, 5·4%). Hydrolysis of the acetyl derivative (2·3 g.) with boiling 2N-hydrochloric acid (25 c.c.) for 30 mins. and neutralisation of the suspension gave *ethyl* 4-p-*sulphanilamidophenyl*-2 : 6-*dimethylpyridine*-3 : 5-*dicarboxylate* (2·0 g.); it separated from dilute alcohol as a solvate, and from benzene it formed small prismatic needles, m. p

164—165° (Found : C, 60·25; H, 5·45. $C_{25}H_{27}O_6N_3S$ requires C, 60·3; H, 5·4%). The corresponding 4-*m*-sulphanilamido-compound was prepared (*a*) similarly in about the same yield from ethyl 4-*m*-aminophenyl-2 : 6-dimethylpyridine-3 : 5-dicarboxylate (Cook, Heilbron, and Steger, *loc. cit.*) and (*b*) from the amine and *p*-nitrobenzenesulphonyl chloride. (*a*) *Ethyl* 4-m-N⁴-*acetylsulphanilamidophenyl*-2 : 6-*dimethylpyridine*-3 : 5-*dicarboxylate* separated from dilute ethanol or acetone–light petroleum in needles, m. p. 196—197° (Found : C, 60·4; H, 5·6. $C_{27}H_{29}O_7N_3S$ requires C, 60·1; H, 5·4%). *Ethyl* 4-m-*sulphanilamidophenyl*-2 : 6-*dimethylpyridine*-3 : 5-*dicarboxylate* formed prisms, m. p. 158—159°, from ethanol (Found : C, 60·45; H, 5·6. $C_{25}H_{27}O_6N_3S$ requires C, 60·3; H, 5·4%). (*b*) The amine (2·0 g.) was kept for 15 hrs. with *p*-nitrobenzenesulphonyl chloride (1·3 g.) in pyridine (5 c.c.), and crude *ethyl* 4-(3′-p-*nitrobenzenesulphonamidophenyl*)-2 : 6-*dimethylpyridine*-3 : 5-*dicarboxylate* precipitated with water (100 c.c.); it separated from benzene–light petroleum (charcoal) in pale yellow prisms, m. p. 150—151° (Found : C, 57·2; H, 5·2. $C_{31}H_{33}O_9N_3S$ requires C, 56·9; H, 4·8%). The nitro-compound (1 g.) was added slowly to a suspension of iron dust (2 g.) in ethanol (6 c.c.) and 15% hydrochloric acid (1 c.c.). The whole was heated on the steam-bath for 2 hrs., and the solutions made alkaline and decolorised with charcoal. Evaporation and neutralisation gave the sulphanilamido-compound identical with that prepared in (*a*).

4-m-N⁴-*Acetylsulphanilamidophenyl*-2 : 6-*dimethylpyridine* was prepared by heating acetylsulphanilyl chloride (6·6 g.) with 4-*m*-aminophenyl-2 : 6-dimethylpyridine (4·5 g.) in pyridine (60 c.c.) for 1 hr. at 100°, and adding water (350 c.c.); recrystallisation from dilute ethanol gave needles, m. p. 267—268° (Found : C, 63·6; H, 5·5. $C_{21}H_{21}O_3N_3S$ requires C, 63·8; H, 5·3%). Hydrolysis was effected only by boiling in 20% aqueous sodium hydroxide for 30 mins. 4-m-*Sulphanilamidophenyl*-2 : 6-*dimethylpyridine* (yield, 5·0 g. or 64% over-all) crystallised from acetone in large prisms, m. p. 269—270° (Found : C, 64·3; H, 5·5. $C_{19}H_{19}O_2N_3S$ requires C, 64·6; H, 5·4%).

Sulphanilamidophenylthiazoles.—*o*-Acetamidobenzonitrile (20 g.) was heated (autoclave) for 1 hr. at 100° with a mixture of ethanol (240 c.c.) and triethanolamine (40 c.c.) previously saturated with hydrogen sulphide at 0°. Filtration and concentration gave *o*-acetamidothiobenzamide (18·6 g.), m. p. 221—222° after crystallisation from ethanol. The thioamide (10 g.), bromoacetone (5· 4c.c.), and ethanol (100 c.c.) were refluxed for 1 hr. On cooling, a hydrobromide separated, from which neutral impurities were extracted with ether and the free base liberated with ice-cold sodium hydroxide solution. Crystallisation from *cyclo*hexanol–light petroleum gave 2-o-*acetamidophenyl*-4-*methylthiazole* in yellow needles (0·2 g.), m. p. 116—117° (Found : C, 62·4; H, 5·2. $C_{12}H_{12}ON_2S$ requires C, 62·1; H, 5·2%). The alkaline solution on acidification yielded 4-thio-2-methyldihydroquinazolone, m. p. 220° (decomp.), identified as its picrate, m. p. 203—205° (Bogert, Breneman, and Hand, *loc. cit.*).

Acetylsulphanilyl chloride (51 g.) was heated with *o*-aminobenzonitrile (24·6 g.) in pyridine (100 c.c.) for 1 hour at 100°. The *product* (59·5 g.), m. p. 217—220°, separated in solvated form from dilute ethanol but in unsolvated needles, m. p. 224°, from acetone–light petroleum (Found : C, 56·9; H, 4·4. $C_{15}H_{13}O_3N_3S$ requires C, 57·1; H, 4·15%). Ethanol (30 c.c.), saturated with ammonia and then with hydrogen sulphide, was heated with the nitrile for 12 hrs. at 100°. Evaporation and addition of water precipitated a solid mixture of the original nitrile and *o*-acetylsulphanilamidothiobenzamide, which was separated by several crystallisations from dilute ethanol, the thioamide, m. p. 200° (decomp.), being obtained from the mother-liquors. The crude thioamide (16 g.) was refluxed for 1 hr. with ethanol (200 c.c.) and bromoacetone (5 c.c.). Removal of solvent in a vacuum, addition of water, and purification of the solid by solution in alkali and precipitation with acid gave 2-o-N⁴-*acetylsulphanilamidophenyl*-4-*methylthiazole* (4·1 g.), which separated from dilute ethanol in prisms, m. p. 168·5—169° (Found : C, 55·7; H, 4·4. $C_{18}H_{17}O_3N_3S_2$ requires C, 55·8; H, 4·4%). Hydrolysis of the acetyl compound (4·0 g.) with boiling 2N-hydrochloric acid (40 c.c.) for 1 hr. and neutralisation (charcoal) gave 2-o-*sulphanilamidophenyl*-4-*methylthiazole* (2·9 g.), which separated from ethanol in large prismatic needles, m. p. 178° (Found : C, 55·8; H, 4·7. $C_{16}H_{15}O_2N_3S_2$ requires C, 55·6; H, 4·4%).

m-Acetamidobenzonitrile (20 g.) was heated for 1 hour with ethanol (240 c.c.) and triethanolamine (40 c.c.) previously saturated with hydrogen sulphide at 0°. Concentration gave crude m-*acetamidothiobenzamide* (16 g.), which separated in prisms, m. p. 177—178° (decomp.), from acetone–light petroleum (Found : C, 55·35; H, 5·2. $C_9H_{10}ON_2S$ requires C, 55·6; H, 5·2%). The thioamide was converted into 2-m-*acetamidophenyl*-4-*methylthiazole* (yield, 57%) as with the *o*-isomeride above; crystallisation from benzene–light petroleum gave prisms, m. p. 130—131° (Found : C, 62·15; H, 5·1. $C_{12}H_{12}ON_2S$ requires C, 62·1; H, 5·2%). Hydrolysis of the acetyl compound (7 g.) with 10 vols. of boiling 6N-hydrochloric acid for 15 mins. and neutralisation of the solution gave 2-m-*aminophenyl*-4-*methylthiazole* (5·5 g.), which separated from light petroleum in small prisms, m. p. 46—48° (Found : C, 63·1; H, 5·3. $C_{10}H_{10}N_2S$ requires C, 63·1; H, 5·3%). Introduction of the acetylsulphanilyl residue and removal of the acetyl group was effected in excellent yield by the methods used in preceding cases. 2-m-N⁴-*Acetylsulphanilamidophenyl*-4-*methylthiazole* formed needles, m. p. 233°, from acetone–light petroleum (Found : C, 56·0; H, 4·6. $C_{18}H_{17}O_3N_3S_2$ requires C, 55·6; H, 4·4%). 2-m-*Sulphanilamidophenyl*-4-*methylthiazole* separated from dilute ethanol in small prisms, m. p. 188—189° (Found : C, 55·7; H, 4·35. $C_{16}H_{15}O_2N_3S_2$ requires C, 55·6; H, 4·4%).

The following appears to be an improvement on existing preparations of thiobenzamide. Benzonitrile (50 g.) was refluxed for 2 hrs. with 16% aqueous ammonium sulphide (300 c.c.) and ethanol (250 c.c.). Evaporation to dryness and crystallisation of the residue three times from water gave the pure compound (35 g.), m. p. 116°. Nitration of 2-phenyl-4-methylthiazole by the method of Friedman, Sparks, and Adam (*loc. cit.*) gave a mixture from which 2-2′ : 4′-*dinitrophenyl*-4-*methylthiazole* was obtained as the less soluble component by fractional crystallisation from *cyclo*hexane; it formed yellow needles, m. p. 154—155° (Found : C, 45·3; H, 2·65. $C_{10}H_7O_4N_3S$ requires C, 45·3; H, 2·65%). 2-4′-Nitrophenyl-4-methylthiazole, m. p. 107°, was conveniently separated from the mixture by its preferential solution in 16% hydrochloric acid; it was evidently identical with the compound described by Friedman, Sparks, and Adam.

2-*p*-Aminophenyl-4-methylthiazole, better prepared *via p*-acetamidothiobenzamide, was converted into the sulphanilyl derivative in the manner of other preparations in this paper. 2-p-N⁴-*Acetylsulphanilamidophenyl*-4-*methylthiazole* (yield, 81%) separated from ethanol in prismatic needles, m. p. 255—256° (Found : C, 55·9; H, 4·45. $C_{18}H_{17}O_3N_3S_2$ requires C, 55·8; H, 4·4%). 2-p-*Sulphanilamidophenyl*-4-*methylthiazole* (yield after crystallisation, 85%) separated from dilute ethanol in needles, m. p. 202—203° (Found : C, 55·4; H, 4·4. $C_{16}H_{15}O_2N_3S_2$ requires C, 55·6; H, 4·4%).

2-*m*-Nitrophenyl-4 : 6-dimethylpyrimidine (Ochiai *et al.*, *loc. cit.*), m. p. 157·5°, was oxidised with a boiling solution of potassium permanganate in acetic acid and 5N-sulphuric acid. *m*-Nitrobenzoic acid, m. p. and mixed m. p. with authentic material 140°, was obtained. The corresponding amine was converted into the sulphonamide in the usual manner. 2-m-N⁴-*Acetylsulphanilamidophenyl*-4 : 6-*dimethylpyrimidine* (yield, theoretical) separated from acetone or a large volume of ethanol in prisms, m. p. 246—248° (Found : C, 60·6; H, 5·2. $C_{20}H_{20}O_3N_4S$ requires C, 60·6; H, 5·1%). 2-m-*Sulphanilamidophenyl*-4 : 6-*dimethylpyridine* (yield, 74% after recrystallisation) formed small prisms, m. p. 206—207°, from dioxan–light petroleum (Found : C, 61·0; H, 5·2. $C_{19}H_{19}O_2N_4S$ requires C, 61·0; H, 5·1%).

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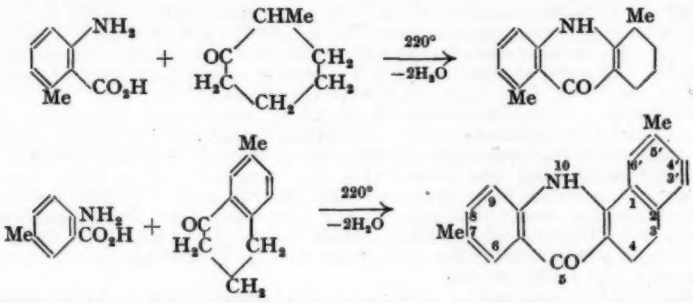
47. *Hydroacridones: Synthesis and Dehydrogenation. Part II.*

By R. A. Reed.

Dimethyltetrahydro-, methyldihydrobenz-, and dimethydihydrobenz-acridones have been prepared by condensation of the five methylanthranilic acids with 2- and 3-methyl*cyclo*hexanone, 1-tetralone, and 7-methyl-1-tetralone at 220°. Dehydrogenation has been effected by heating in air with copper powder at 360—400°. Orientation of the dimethylacridones has been established by absolute methods and by examination of their ultra-violet fluorescence colours.

Dimethyltetrahydroacridones, methyl- and dimethyl-dihydrobenzacridones have been prepared and dehydrogenated by methods similar to those used for methyltetrahydroacridones (J., 1944, 425).



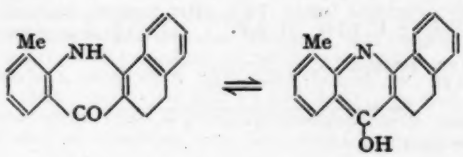
Only dimethyl-1 : 2 : 3 : 4-tetrahydroacridones containing both methyl groups in the same benzene ring have hitherto been described (Hughes and Lions, *Proc. Roy. Soc. N.S. Wales*, 1937, **71**, 458; Sen and Basu, *J. Indian Chem. Soc.*, 1930, **7**, 435; Huggill and Plant, J., 1939, 784), being prepared by condensation of the appropriate xylidine with ethyl *cyclo*hexenone-2-carboxylate, followed by cyclisation of the resultant anil at 260—280°. No dihydro-1 : 2-benzacridone derivatives have hitherto been described, although Bukhsh and Desai (*Proc. Indian Acad. Sci.*, 1939, **10**, *A*, 262) condensed anthranilic acid with *trans*-2-ketodecahydronaphthalene to obtain an octahydrobenzacridone of undetermined orientation.

The dimethyltetrahydroacridones obtained by using 3-methyl*cyclo*hexanone may contain this methyl group in either the 2- or the 4-position. Only one product has been isolated and this contains the methyl group in the 2-position. The orientation has been established in some cases by dehydrogenation and comparison of the resulting dimethylacridone with one of known orientation prepared by similar means. Thus 2 : 9-dimethylacridone may also be prepared by condensation of 4-methylanthranilic acid with 2-methyl*cyclo*hexanone and dehydrogenation of the product.

Examination under ultra-violet light of alcoholic solutions of the dimethylacridones produced on dehydrogenation, when made acid and alkaline by the addition of a few drops of 5N-hydrochloric acid and sodium hydroxide respectively, shows that a methyl group in position 4 or 6, *i.e.*, adjacent to the carbonyl group, results in both the acid and the alkaline solution fluorescing green. A methyl group in position 10 gives rise to a green colour in acid and a blue in alkaline solution. Methyl groups in any other positions give the normal acridone colours, *viz.*, blue in acid, green in alkali. On this evidence, the products arising from 3-methyl*cyclo*hexanone have the unfixed methyl group in position 2 and not 4. Obviously, however, when 6-methylanthranilic acid is condensed with the ketone, such evidence cannot determine the orientation of the dehydrogenated product. It is noteworthy that 4 : 10-dimethylacridone gives fluorescence colours similar to those of 10- and not 4-methylacridone, showing that the methyl group in position 10 has greater control over the fluorescence colours exhibited. By contrast, all the 1 : 2-benzacridone derivatives described show precisely the same colours, *viz.*, green in acid, blue in alkali. In this case, therefore, a methyl group in position 6 has no effect upon the colour given. The 1 : 2-benzacridones, when dissolved in alcohol, show only a faint blue-violet daylight fluorescence as opposed to the relatively strong fluorescence of the methyl- and dimethyl-acridones.

The dimethyltetrahydroacridones now reported are all soluble in dilute hydrochloric acid and give insoluble dichromates. Their solutions in cold concentrated sulphuric acid are yellow, showing no daylight fluorescence, unlike the hydroacridones containing three benzene rings, which yield yellow solutions exhibiting a blue or bluish-green fluorescence.

Only those methyl- or dimethyl-dihydrobenzacridones having a methyl group in position 9 are soluble in dilute acid, showing that the adjacent electron-repelling methyl group sends the equilibrium further towards the hydroxyacridine structure postulated by Tiedtke (*Ber.*, 1909, **42**, 621) for 1 : 2 : 3 : 4-tetrahydroacridone itself.



The introduction of a methyl group in position 9 generally has a marked lowering effect upon the melting point of both the hydroacridone and its dehydrogenation products.

All the hydroacridones described are soluble in alcoholic alkali except 10-phenyl-1 : 2 : 3 : 4-tetrahydroacridone; 2 : 10-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone is, however, easily soluble in alcohol alone, as is 10-methyltetrahydroacridone (see Part I, *loc. cit.*). All the hydroacridones are insoluble in aqueous alkali, as are also the acridones obtained from them.

Experimental.

All m. p.'s recorded (liquid paraffin bath) are corrected and all nitrogen analyses (micro-Dumas) are by Dr. G. Weiler of Oxford.

1 : 9-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—3-Methylanthranilic acid (Part I, *loc. cit.*) (10 g.) and 2-methyl*cyclo*hexanone (93%; 12·5 ml.) were heated at 220° for 1½ hours. The liquid residue (solid when cold) was dissolved in boiling alcohol (25 ml.) and allowed to cool. The crystals were collected, washed with alcohol and with ether (yield, 5·7 g.; 40%), and recrystallised from alcohol (norit), giving almost colourless needles, m. p. 193—194°. The picrate, prepared in xylene solution and recrystallised from acetic acid, had m. p. 191—192° (decomp.). Titration of this with N/10-sodium hydroxide, and ethyl bis-2 : 4-dinitrophenylacetate as indicator, showed *M* for the base 225 (Calc. for $C_{15}H_{17}ON$: *M*, 227).

1 : 8-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—A mixture of 4-methylanthranilic acid (4 g.) and 2-methyl*cyclo*hexanone (93%; 5 ml.) was heated at 220° for 1½ hours. The cold solid residue was boiled with alcohol (10 ml.), cooled, filtered off, and washed with alcohol and ether (yield, 1·15 g.; 19%). The product crystallised from pyridine in cream-coloured prisms, m. p. 325°. The picrate separated overnight from alcohol in yellow needles, m. p. 204—206° (decomp.), titration indicating *M* for the base 228.

1 : 7-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—5-Methylanthranilic acid (7 g.) and 2-methyl*cyclo*hexanone (93%; 8 ml.), heated and worked up as above, gave 3·5 g. (34%) of crude product. This on recrystallisation from pyridine gave cream plates, m. p. 339°. Titration of the picrate, yellow prisms from acetic acid, m. p. 165—167° (decomp.), indicated *M* for the base 227.

1 : 6-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—From 2 g. of 6-methylanthranilic acid and 3 ml. of 2-methyl*cyclo*hexanone (93%), heated at 210° for 2½ hours, the crude product, isolated as before, amounted to 0·7 g. (23%). Recrystallisation from pyridine gave cream crystals, m. p. 311° (Found: N, 6·2. $C_{15}H_{17}ON$ requires N, 6·2%).

2 : 9-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—A yield of 3·2 g. (53%) of crude product was obtained from 4 g. of 3-methylanthranilic acid and 5 ml. of 3-methyl*cyclo*hexanone (98%) after 2½ hours' heating at 210°. Recrystallisation from pyridine gave cream-coloured crystals, m. p. 326°. Titration of the picrate, m. p. 218° (decomp.) (from acetic acid), indicated for the base *M* 227.

2 : 8-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—This was obtained (yield, 1·8 g.; 30%) from 4 g. of 4-methylanthranilic acid and 5 ml. of 3-methyl*cyclo*hexanone (98%) after 1 hour at 220°. Recrystallisation from much pyridine gave cream needles, m. p. above 385°. The hydrochloride crystallised when a hot solution in 2N-hydrochloric acid cooled. Titration of the picrate, m. p. 222° (from alcohol), gave *M* for the base 228.

2 : 7-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—This was produced by heating a mixture of 6 g. of 5-methylanthranilic acid and 8 ml. of 3-methyl*cyclo*hexanone (98%) at 220° for 30 mins. (yield, 4·2 g.; 40%). Recrystallisation from much pyridine gave colourless or faintly pink leaflets, m. p. 378°. This compound rapidly dissolved in 5N-hydrochloric acid, the hydrochloride soon separating. The picrate, m. p. 222° (decomp.) (from acetic acid), showed on titration *M* for the base 223.

2 : 6-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—Heated at 220° for 1½ hours, a mixture of 2 g. of 6-methylanthranilic acid and 3 ml. of 3-methyl*cyclo*hexanone (98%) gave this *compound* (0·8 g.; 27%). Colourless prisms, m. p. 365°, were obtained by recrystallisation from pyridine (Found: N, 6·2. $C_{15}H_{17}ON$ requires N, 6·2%). The picrate separated from acetic acid in yellow crystals, m. p. 168° (decomp.), containing acetic acid of crystallisation.

2 : 10-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—This was obtained (4·5 g.; 32%) from 10 g. of *N*-methylanthranilic acid (Part I, *loc. cit.*) and 12·5 ml. of 3-methyl*cyclo*hexanone (98%) at 220° for 2 hours, with crystallisation of the residue from 40 ml. of benzene. Recrystallisation from pyridine gave colourless crystals, m. p. 192—193°, becoming brownish on exposure and readily soluble in cold alcohol. The picrate, m. p. 173—174° (from acetic acid), gave, on titration, *M* for the base 229.

An attempt to prepare 1 : 10-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone from *N*-methylanthranilic acid and 2-methyl*cyclo*hexanone (93%) gave no solid product.

10-*Phenyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—Two hours' heating at 210° of a mixture of 10 g. of *N*-phenylanthranilic acid (*Org. Synth.*, **19**, 6) and 8 g. of *cyclo*hexanone (97·5%) and treatment of the residue with 100 ml. of benzene gave 3·5 g. (28%) of product. Recrystallisation from alcohol (norit) gave pale yellow prisms, m. p. 298°, insoluble in cold alcoholic alkali but soluble in fairly concentrated sulphuric acid, dilution precipitating the base. The solution in cold concentrated sulphuric acid showed a fluorescence (bluish-green). Titration of the picrate, m. p. 142° (from acetic acid), indicated *M* for the base 277 (Calc. for $C_{19}H_{17}ON$: *M*, 275).

Dehydrogenations.—These were accomplished by heating in a metal-bath with 2 parts of copper powder at 360—400° as described in Part I. The total sublimate was extracted with boiling 2N-hydrochloric acid, and the insoluble solid recrystallised from a suitable solvent.

1 : 9-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·1 g. of 1 : 9-*dimethylacridone*, yellow leaflets, m. p. 230°, after recrystallisation from alcohol (Found: N, 6·4. $C_{15}H_{13}ON$ requires N, 6·3%). 1 : 8-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·45 g.) gave 0·1 g. of 1 : 8-*dimethylacridone*, pale yellow needles, m. p. 301°, after two crystallisations from pyridine (Found: N, 6·55%). 1 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·4 g.) gave 0·2 g. of 1 : 7-*dimethylacridone*, pale yellow needles, m. p. 343° after crystallisation from pyridine (Found: N, 6·8%), and 1 : 6-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) yielded 0·2 g. of 1 : 6-*dimethylacridone*, pale yellow needles, m. p. 282° after recrystallisation from 50% pyridine (Found: N, 6·3%).

2 : 9-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) yielded 0·15 g. of product, pale yellow crystals, m. p. 314°, from pyridine (Found: N, 6·3%). A mixed m. p. with 1 : 8-dimethylacridone gave m. p. 301°, *i.e.*, no depression, and the ultra-violet fluorescence colours were identical. On this evidence 1 : 8-dimethylacridone would appear to be dimorphic.

2 : 8-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·15 g. of product, yellow needles, m. p. 363°, from aqueous pyridine (Found: N, 6·45%). Since the ultra-violet fluorescence colours were blue in acid, green in alkali, the product was 2 : 8-*dimethylacridone*.

2 : 7-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) produced 0·1 g. of yellow needles, m. p. 328° (from alcohol) (Found: N, 6·55%). The fluorescence colours, blue in acid, green in alkali, show the product to be 2 : 7-*dimethylacridone*.

2 : 6-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·3 g.) yielded 0·1 g. of a product, pale yellow needles, m. p. 352°, from

pyridine (Found: N, 6·1%). In this case the fluorescence colours, green in acid, green in alkali, cannot confirm the orientation, but the high m. p. is evidence for 2 : 6-*dimethylacridone*.

2 : 10-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·05 g. of 2 : 10-dimethylacridone, m. p. 181°, after two crystallisations from aqueous alcohol and one from benzene. A specimen prepared by methylation of 2-methylacridone (Gleu and Nitzsche, *J. pr. Chem.*, 1939, **153**, 219) had the same m. p., and a mixture of the two showed no depression. The fluorescence colours were green in acid, blue in alkali.

10-Phenyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·2 g. of 10-phenylacridone, buff-coloured prisms, m. p. 275° (decomp.), from toluene (Goldberg and Nimerovsky, *Ber.*, 1907, **40**, 2450, record m. p. 276°). The colours given under ultra-violet light were bluish-green in acid, blue in alkali.

To establish the validity of the fluorescence technique in these orientation problems, the monomethylacridones (see Part I), 3 : 10- and 4 : 10-dimethylacridone (Gleu and Nitzsche, *loc. cit.*) were examined in alcoholic solution under ultra-violet light.

	Acid.	Alkali.		Acid.	Alkali.
Acridone	Blue	Green	4-Methylacridone	Green	Green
1-Methylacridone	,,	,,	10-Methylacridone	,,	Blue
2-Methylacridone	,,	,,	3 : 10-Dimethylacridone	,,	,,
3-Methylacridone	,,	,,	4 : 10-Dimethylacridone	,,	,,

That these rules do not apparently apply where the substituent groups in the acridone nucleus are other than methyl is shown by the fact that 2-chloro-7-methoxyacridone (May and Baker Ltd.) showed green fluorescence in acid and also in alkali.

3 : 4-*Dihydro*-1 : 2-*benzacridone*.—A mixture of 7 g. of anthranilic acid and 11 g. of 1-tetralone (Schroeter, D.R.P. 346,948; *p*-nitrophenylhydrazone, m. p. 231—232°) was heated to 200° during 1½ hours and maintained at 220° for a further hour. The residue was refluxed for 1½ hours with 50 ml. of benzene, cooled, and filtered. The solid was washed with pyridine to remove colour and then with ether, giving a yield of 5·4 g. (43%). Recrystallisation from acetic acid gave cream needles, m. p. 301°. Titration of the picrate, m. p. 175°, prepared in acetic acid solution and dried at 100°, gave *M* for the base 247 (Calc. for $C_{17}H_{13}ON$: *M*, 247).

9-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—3-Methylanthranilic acid (4 g.) and 1-tetralone (5 g.) were heated at 220° for 2½ hours, and the product extracted with 20 ml. of alcohol. The residue (2·5 g.; 36%), recrystallised from alcohol, gave cream leaflets, m. p. 216°. The picrate, m. p. 191—192°, prepared in alcohol and dried at 100°, showed on titration *M* for the base 264 (Calc. for $C_{18}H_{15}ON$: *M*, 261).

8-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—A mixture of 4 g. of 4-methylanthranilic acid and 6 g. of 1-tetralone, heated at 220° for 1½ hours, gave 1·8 g. (26%) of product, after extraction with alcohol. Recrystallisation of the brownish prisms from much pyridine gave cream prisms, m. p. 320° (Found: N, 5·8. $C_{18}H_{15}ON$ requires N, 5·4%).

7-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—5-Methylanthranilic acid (2 g.) and 1-tetralone (2·2 g.; 1·15 mols.), heated at 220—240° for ½ hour and extracted with benzene, gave a yield of 1·6 g. (46%). Recrystallisation from pyridine gave cream needles, m. p. 319°. Titration of the picrate, m. p. 199° (decomp.) (from acetic acid, and dried at 100°), indicated *M* for the base 262 (Calc., 261).

6-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—A mixture of 2 g. of 6-methylanthranilic acid and 2·5 g. of 1-tetralone was heated at 220° for 1½ hours. The cold liquid residue was heated with 10 ml. of benzene and allowed to cool; 0·75 g. (22%) of product then separated. Recrystallisation from pyridine–alcohol gave colourless needles, m. p. 257—258° (Found: N, 5·5. $C_{18}H_{15}ON$ requires N, 5·4%).

5′-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—One hour's heating at 220° of a mixture of 7 g. of anthranilic acid and 11 g. of 7-methyl-1-tetralone (Barnett and Sanders, J., 1933, 434; see also Fieser and Martin, *Org. Synth.*, **15**, 92; Martin, *ibid.*, **17**, 97; *p*-nitrophenylhydrazone, m. p. 192—193°) gave 5·8 g. (43·5%) of product after extraction with 50 ml. of benzene. Recrystallisation from pyridine produced cream needles, m. p. 300°. Titration of the picrate, m. p. 207° (from acetic acid), showed *M* for the base 255 (Calc., 261).

5′ : 9-*Dimethyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—3-Methylanthranilic acid (4 g.) and 7-methyl-1-tetralone (5 g.) were heated together at 220° for 2½ hours, and the residue extracted with 20 ml. of alcohol and washed with a little pyridine, alcohol, and finally ether. Recrystallisation of the product (2·7 g.; 37%) from dilute acetic acid yielded colourless needles, m. p. 240°. Titration of the picrate, m. p. 206—207° (from alcohol), showed *M* for the base 279 (Calc., 275). The picrate, prepared in acetic acid solution, had m. p. 187—188° and contained solvent of crystallisation.

5′ : 8-*Dimethyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—A yield of 4·0 g. (55%) was obtained as a brown crystalline solid from a mixture of 4 g. of 4-methylanthranilic acid and 7 g. of 7-methyl-1-tetralone by heating at 220° for 1½ hours and extracting the product with 100 ml. of alcohol. Recrystallisation from pyridine (norit) gave cream needles, m. p. 299° (Found: N, 5·4. $C_{19}H_{17}ON$ requires N, 5·1%). The picrate, m. p. 229° (decomp.) (from acetic acid), is not equimolecular.

5′ : 7-*Dimethyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—A mixture of 4 g. of 5-methylanthranilic acid and 5 g. of 7-methyl-1-tetralone, heated and worked up as for the 5′ : 9-compound, gave 4·7 g. (65%) of product, which crystallised from pyridine in cream needles, m. p. 304°. Titration of the picrate, m. p. 216° (decomp.) (from acetic acid), indicated *M* for the base 277 (Calc., 275).

5′ : 6-*Dimethyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—6-Methylanthranilic acid (2 g.) and 7-methyl-1-tetralone (2·5 g.), heated at 220° for 1½ hours and extracted with 10 ml. of benzene, gave 1·0 g. (28%) of product as grey prisms. Recrystallisation from pyridine yielded colourless crystals, m. p. 303—304° (Found: N, 5·3. $C_{19}H_{17}ON$ requires N, 5·1%).

Dehydrogenations.—3 : 4-Dihydro-1 : 2-benzacridone (0·5 g.) gave 0·1 g. of 1 : 2-benzacridone, pale yellow needles, m. p. above 380°, from pyridine (Ullmann and Rasetti, *Annalen*, 1907, **355**, 351, give m. p. above 360°).

9-Methyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) yielded 0·05 g. of 9-*methyl*-1 : 2-*benzacridone*, pale yellow needles, m. p. 265°, from aqueous pyridine (Found: N, 5·4. $C_{18}H_{13}ON$ requires N, 5·4%), 8-methyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) produced 0·1 g. of 8-*methyl*-1 : 2-*benzacridone*, m. p. 364°, pale yellow needles from pyridine (Found: N, 5·75%), 7-methyl-3 : 4-dihydro-1 : 2-benzacridone (0·35 g.) gave 0·15 g. of 7-*methyl*-1 : 2-*benzacridone*, m. p. 378—379°, pale yellow needles from pyridine (Found: N, 5·65%), 6-methyl-3 : 4-dihydro-1 : 2-benzacridone (0·4 g.) yielded 0·2 g. of 6-*methyl*-1 : 2-*benzacridone*, m. p. 286°, pale yellow needles from 50% pyridine (Found: N, 5·3%), and 5′-methyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) gave rise to 0·15 g. of 5′-*methyl*-1 : 2-*benzacridone*, m. p. 341°, pale yellow needles from aqueous pyridine (Found: N, 6·0%).

5′ : 9-Dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) produced 0·04 g. of 5′ : 9-*dimethyl*-1 : 2-*benzacridone*, m. p. 238°, yellow crystals from aqueous alcohol (Found: N, 5·4. $C_{19}H_{15}ON$ requires N, 5·1%), 5′ : 8-dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·4 g.) gave 0·1 g. of 5′ : 8-*dimethyl*-1 : 2-*benzacridone*, m. p. 320°, pale yellow needles from aqueous pyridine (Found: N, 4·95%), 5′ : 7-dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) produced 0·2 g. of 5′ : 7-*dimethyl*-

1 : 2-*benzacridone*, m. p. 334°, pale yellow needles from aqueous pyridine (Found : N, 4·75%), and 5′ : 6-dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·4 g.) yielded 0·05 g. of 5′ : 6-*dimethyl*-1 : 2-*benzacridone*, m. p. 276°, pale yellow needles from 50% pyridine (norit) (Found : N, 5·0%).

My thanks are due to the Directors of Messrs. Hopkin and Williams Ltd. for facilities and for permission to publish these results.

RESEARCH LABORATORY, HOPKIN AND WILLIAMS LTD., LONDON, E.C. 1. [*Received, October 17th*, 1944.]

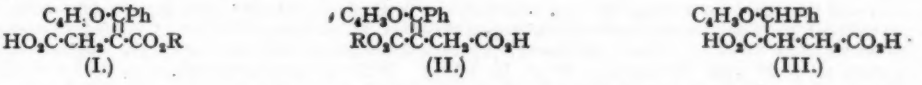
48. *Intramolecular Ring Closures with* cis- *and* trans-*γ-Phenyl-γ-(2-furyl)itaconic Acid.**

By EDWARD B. KNOTT.

cis- and trans-*γ-Phenyl-γ-(2-furyl)itaconic acid* have been prepared by the condensation of ethyl succinate with phenyl 2-furyl ketone. The *cis*-acid has been cyclised to 4-*hydroxy*-7-*phenylcoumarone*-2-*carboxylic acid* and 1-*keto*-3-(2′-*furyl*)*indene*-2-*acetic acid*, both of which give 2-*hydroxy*-9-*keto*-3′ : 2′ : 3 : 4-*furofluorene* on further cyclisation. The *trans*-acid underwent ring closure to 1-*hydroxy*-4-(2′-*furyl*)*naphthalene*-3-*carboxylic acid*.

THE synthesis of 1-hydroxy-4-phenylnaphthalene-3-carboxylic acid was effected by Borsche and his school (*Annalen*, **1936**, **526**, 1) by intramolecular ring closure of the monoester of γγ-diphenylitaconic acid. The cyclisation of the dibasic acid was achieved by Stobbe and Vieweg (*Ber.*, 1902, **35**, 1727), who obtained 1-keto-3-phenylindene-2-acetic acid, which was cyclised by Borsche (*loc. cit.*) to 2-hydroxy-3 : 4-benzfluorenone. This fluorenone has now been found to function as a colour coupler, giving on development of a photographic emulsion with dialkyl-*p*-phenylenediamines a black dye image. It was thought to be of interest, therefore, to prepare other fluorenones of this type.

This work follows the same line of reactions as the above, but by the replacement of one of the phenyl groups of the itaconic acid by a furyl group, two isomeric itaconic acids were to be expected which could lead to two series of cyclisation products. The initial materials were obtained by the condensation of phenyl 2-furyl ketone with ethyl succinate under the influence of alcoholic sodium ethoxide. Depending on the conditions of condensation, two isomeric products were isolated, *ethyl hydrogen* cis-*γ-phenyl-γ-(2-furyl)itaconate* (I; R = Et) and the trans-*isomer* (II; R = Et).

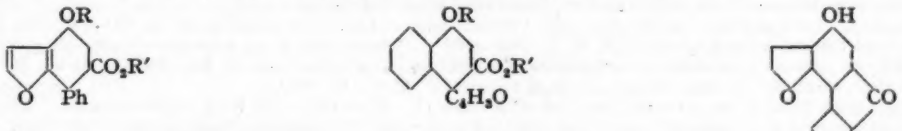


(I.) (II.) (III.)

Hydrolysis of these products yielded cis- and trans-*γ-phenyl-γ-(2-furyl)itaconic acids* (I and II; R = H). On reduction with sodium amalgam the acids yielded what are believed to be the isomeric forms of *γ-phenyl-γ-(2-furyl)pyroracemic acid* (III). This acid contains two asymmetric carbon atoms and can give two racemates.

The analysis of the acids indicates in both cases the presence of water of crystallisation, which is difficult to remove. The addition of elements of water to the furan ring during reduction, leading to an aldehyde, is unlikely, as the acids exhibit no reducing properties. No ring closures have been attempted with (III).

The ethyl hydrogen esters (I) and (II) were readily cyclised by acetic anhydride–sodium acetate, the *cis*-ester giving *ethyl* 4-*acetoxy*-7-*phenylcoumarone*-6-*carboxylate* (IV; R = Ac, R′ = Et) and the *trans*-ester giving *ethyl* 1-*acetoxy*-4-(2′-*furyl*)*naphthalene*-3-*carboxylate* (V; R = Ac; R′ = Et).



(IV.) (V.) (VI.)

The identity of the ethyl hydrogen esters and their cyclisation products was shown by oxidation of (IV) and (V) with permanganate; the former gave an almost theoretical yield of benzoic acid, but the latter gave no identifiable product.

(IV) and (V) gave on mild hydrolysis *ethyl* 4-*hydroxy*-7-*phenylcoumarone*-6-*carboxylate* (IV; R = H, R′ = Et) and *ethyl* 1-*hydroxy*-4-(2′-*furyl*)*naphthalene*-3-*carboxylate* (V; R = H, R′ = Et) respectively. Further hydrolysis yielded 4-*hydroxy*-7-*phenylcoumarone*-6-*carboxylic acid* (IV; R = R′ = H) and 1-*hydroxy*-4-(2′-*furyl*)-*naphthalene*-3-*carboxylic acid* (V; R = R′ = H). The acids were characterised by their *acetyl* derivatives. Both (IV) and (V) (R = H) coupled normally with diazonium salts to give red dyes.

Further cyclisation of (IV; R = R′ = H) with concentrated sulphuric acid gave 2-*hydroxy*-9-*keto*-3′ : 2′ : 3 : 4-*furofluorene* (VI), purified and obtained crystalline through its *acetyl* derivative.

* Patent pending.

Alternatively (IV; R = Ac, R′ = H) was converted into its *acid chloride* and *anhydride* and cyclised by aluminium chloride, yielding the acetyl derivative of (VI).

The sodium salt of (VI) is distinguished by its deep purple colour, corresponding to the blue sodium salt of the hydroxybenzfluorenone of Borsche (*loc. cit.*). Various derivatives of (VI) were formed, including the acetate, the *benzoate*, and the *methyl ether*, and its *oxime*. (VI) functioned as a colour coupler in photographic developers, forming with the oxidation product of dialkyl-*p*-phenylenediamines a warm brown dye image (patent pending).

Attempts further to cyclise (V; R′ = H) gave no crystalline products.

From the *cis*-phenylfurylitaconic acid (I; R = H) a good yield of 1-*keto*-3-(2′-*furyl*)*indene*-2-*acetic acid* was obtained on cyclisation with cold concentrated sulphuric acid. It was characterised by its 2 : 4-*dinitrophenylhydrazone*, and on refluxing with acetic anhydride–sodium acetate gave an excellent yield of the acetyl derivative of (VI).

The *trans*-phenylfurylitaconic acid could not be cyclised.

Experimental.

Analyses are by Drs. Weiler and Strauss, Oxford. M. p.'s are corrected. The majority of the compounds have a softening-melting range rather than a sharp m. p., even after repeated crystallisation.

Phenyl furyl ketone, prepared according to Marquis (*Ann. Chim. Phys.*, 1905, **4**, 276) from furoyl chloride, distilled at 285°/760 mm.

Ethyl Hydrogen cis-*γ*-*Phenyl*-*γ*-(2-*furyl*)*itaconate* (I; R = Et).—A mixture of phenyl furyl ketone (68·8 g.; 0·4 mol.) and ethyl succinate (66·7 c.c.; 0·4 mol.) was added in a thin stream, with shaking, to a warm solution of sodium ethoxide (18·4 g.; 0·8 mol. of sodium) in absolute alcohol; it turned red and partly gelled. The whole was heated on the water-bath for ½ hour, and water then added until no more oil was precipitated. The oil, consisting of neutral components, was removed in ether, and the alkaline solution acidified. The oil thus precipitated was dissolved in ether and dried (sodium sulphate), and the ether removed. The yellow-brown oil slowly formed a mass of oil-soaked crystals. These were separated from the oil (40 g.; not further examined) by filtration and washed with a little ether (yield, 40 g.; 33% of the theoretical). Recrystallised from aqueous acetone, they gave lustrous flat needles, m. p. 154—156° after softening at 149° (Found: C, 68·0; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%). With concentrated sulphuric acid a blood-red solution was formed.

Ethyl Hydrogen trans-*γ*-*Phenyl*-*γ*-(2-*furyl*)*itaconate* (II; R = Et).—A mixture of phenyl furyl ketone (100 g.; 0·58 mol.) and ethyl succinate (95 c.c.; 0·58 mol.) was shaken at room temperature with a solution of sodium ethoxide (26·5 g.; 1·16 mols. of sodium) in an excess of absolute alcohol. After 12 hours, the whole was heated on the water-bath for 15 minutes, and water added. The precipitated neutral oil was removed in ether, and the alkaline solution neutralised with dilute hydrochloric acid. The oil thus precipitated solidified completely (yield, 109 g.). (If the alkaline solution was acidified, the oil only partly solidified, possibly owing to precipitation of an oily by-product by the excess of acid.) The cake was broken up, dried in a vacuum, and dissolved in methylene chloride, and ligroin gradually added. The first crop of crystals (10 g.) consisted of the ethyl hydrogen *cis*-ester, m. p. 154—156°, and the second crop (70 g.), m. p. 93—96°, of the *trans*-form (27·5%). Recrystallised from benzene–ligroin, the *ethyl hydrogen* trans-*ester* formed light fawn needle clusters, m. p. 93—96° (Found: C, 68·2; H, 5·4%). With concentrated sulphuric acid a blood-red solution was formed.

cis-*γ*-*Phenyl*-*γ*-(2-*furyl*)*itaconic Acid* (I; R = H).—A solution of the ethyl hydrogen *cis*-ester (5 g.) in 2·5% aqueous potassium hydroxide (200 c.c.) was boiled for 1 hour, acidified while hot, and allowed to cool. The crystals obtained were recrystallised from methanol–hot water, the cis-*acid* forming colourless prisms (4 g.), m. p. 208—215° (decomp.) (Found: C, 65·9; H, 4·5. $C_{15}H_{12}O_5$ requires C, 66·1; H, 4·5%).

trans-*γ*-*Phenyl*-*γ*-(2-*furyl*)*itaconic Acid* (II; R = H).—The ethyl hydrogen *trans*-ester was treated similarly. Acidification produced a yellow oil, which slowly crystallised. From benzene, the trans-*acid* formed fawn prisms (4·1 g.), m. p. 148—154° (Found: C, 66·4; H, 4·5%).

Reduction of cis- *and* trans-*Phenylfurylitaconic Acids: γ*-*Phenyl*-*γ*-(2-*furyl*)*pyroracemic Acids* (III).—10% Sodium amalgam (30 g.) was added during 6 hours to a solution of the acid (0·2 g.) in 10% aqueous sodium hydroxide (100 c.c.) heated on the water-bath, carbon dioxide being passed over the surface. The solution was decanted, the mercury washed, and the combined aqueous solutions filtered and acidified. From both acids, bulky white precipitates were obtained, which were washed with water and recrystallised from hot water.

The *pyroracemic acid* from the *cis*-itaconic acid formed balls of fine silky needles, m. p. 93—98°, and that from the *trans*-itaconic acid formed long silky needles, m. p. 103—108°. The mixed m. p. was never lower than 93—98°. Both acids contained one molecule of water of crystallisation (Found: for acid of m. p. 93—98°, C, 61·6; H, 5·5; for *acid* of m. p. 103—108°, C, 62·0; H, 5·6. $C_{15}H_{14}O_5,H_2O$ requires C, 61·6; H, 5·5%).

Ring Closures with Ethyl Hydrogen cis-*Phenylfurylitaconate* (I; R = Et).—(a) *With sulphuric acid.* The ester (0·5 g.) was dissolved in ice-cold concentrated sulphuric acid (10 c.c.), and the deep red solution kept at 4° for 20 hours and poured into water; red flocks formed which could not be crystallised. They gave a dirty brown dinitrophenylhydrazone, which also could not be obtained crystalline.

(b) *With acetic anhydride.* A mixture of the ester (61·0 g.), anhydrous sodium acetate (40 g.), and acetic anhydride (210 c.c.) was boiled for 3 hours, the yellow liquor concentrated in a vacuum, and the remaining anhydride decomposed with water. The yellow oil slowly crystallised. The yield of crude *ethyl* 4-*acetoxy*-7-*phenylcoumarone*-6-*carboxylate* (IV; R = Ac, R′ = Et) was almost theoretical. Recrystallised from methanol, it formed white crystal aggregates, m. p. 105—108°. It fluoresced blue in ultra-violet light (Found: C, 70·3; H, 4·9. $C_{19}H_{16}O_5$ requires C, 70·35; H, 5·0%).

Ethyl 4-*hydroxy*-7-*phenylcoumarone*-6-*carboxylate* (IV; R = H, R′ = Et) was readily obtained on acidification of the solution obtained by dissolving the acetoxy-derivative in spirit and adding an excess of warm 5% aqueous sodium hydroxide. From hot dilute acetic acid, it formed colourless needles, m. p. 178—181°; these absorbed ultra-violet light strongly (Found: C, 71·85; H, 5·1. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%).

4-*Hydroxy*-7-*phenylcoumarone*-6-*carboxylic Acid* (IV; R = R′ = H).—The crude acetoxy-ester (4·5 g.) was dissolved in spirit (10 c.c.) and boiled for 2 hours with 4% aqueous potassium hydroxide (50 c.c.). The solution was concentrated to half its volume in a vacuum, diluted to 100 c.c. with water, and acidified while hot. The yellow oil obtained soon solidified. From dilute acetic acid, it formed buff-coloured flat needles, m. p. 214—217°, containing ½ mol. of water of crystallisation, removable by heating above 110° for 3 hours (Found: C, 68·6; H, 4·15. $C_{15}H_{10}O_4,\frac{1}{2}H_2O$ requires C, 68·4; H, 4·2%). The red dye obtained by coupling with diazotised aniline formed red spears, m. p. 230—236° (decomp.), from chloroform.

4-Acetoxy-7-phenylcoumarone-6-carboxylic acid (IV; R = Ac, R′ = H) was formed on warming (IV; R = R′ = H) with acetic anhydride and sodium acetate for 5 minutes on the water-bath. It crystallised from methanol in colourless prisms which effloresced, releasing methanol of crystallisation. Dried at 100°/20 mm. for 2 hours, it formed a colourless powder, m. p. 236—238° (Found: C, 68·8; H, 4·15. $C_{17}H_{12}O_6$ requires C, 68·9; H, 4·1%).

Ring Closure of 4-Hydroxy-7-phenylcoumarone-6-carboxylic Acid.—The coumarone (5 g.) was dissolved in ice-cold concentrated sulphuric acid (100 c.c.) and after 15 minutes the green solution was poured into ice-water, and the flocculent brick-red precipitate collected and washed. The crude fluorenone could not be crystallised, so it was acetylated by solution in hot acetic anhydride and sodium acetate, giving, on recrystallisation from methanol, golden needles of *9-keto-2-acetoxy-3′ : 2′ : 3 : 4-furofluorene*, m. p. 169—171° (Found: C, 73·5; H, 3·7. $C_{17}H_{10}O_6$ requires C, 73·4; H, 3·6%). The *2 : 4-dinitrophenylhydrazone* formed orange needles, m. p. 278—280°, from chloroform (Found: N, 12·45. $C_{23}H_{14}O_7N_4$ requires N, 12·2%).

When an alcoholic solution of the acetoxy-derivative was warmed with an excess of sodium hydroxide, the yellow solution became deep purple. It was neutralised, and the red precipitate collected and crystallised from glacial acetic acid, forming blood-red plates, m. p. 221—227°, of *2-hydroxy-9-keto-3′ : 2′ : 3 : 4-furofluorene* (VI) (Found: C, 76·8; H, 3·7. $C_{15}H_{10}O_3$ requires C, 76·2; H, 3·4%). The sodium salt formed purple needles or spears.

Ring Closure of 4-Acetoxy-7-phenylcoumarone-6-carboxylic Acid: 9-Keto-2-acetoxy-3′ : 2′ : 3 : 4-furofluorene.—(a) *With aluminium chloride and the acid chloride.* The acetoxy-derivative (2 g.) was covered with thionyl chloride (10 c.c.) and warmed, hydrogen chloride being briskly evolved. The excess of thionyl chloride was distilled, and the residue, which soon solidified to a yellow crystalline cake, recrystallised from benzene. The *acid chloride* formed colourless needles, m. p. 157—160° (Found: Cl, 11·3. $C_{17}H_{11}O_4Cl$ requires Cl, 11·3%). It was dissolved in carbon disulphide (20 c.c.), aluminium chloride (2 g.) added, and the mixture warmed for 1 hour on the water-bath. The carbon disulphide was driven off, and the black residue decomposed with dilute hydrochloric acid. The yellow flocks (1·2 g.) crystallised from methanol in yellow needles, m. p. 169°, identical with the acetyl derivative of (VI) obtained from the sulphuric acid cyclisation product.

(b) *With aluminium chloride and the anhydride.* The acetylated acid (2 g.) and acetyl chloride (15 c.c.) were warmed until evolution of hydrogen chloride ceased; the excess of solvent was then removed in a vacuum, leaving an oil which soon crystallised. Recrystallised from benzene, the *anhydride* formed colourless plates, m. p. 110—114° (Found: C, 70·9; H, 3·8. $C_{34}H_{22}O_9$ requires C, 71·1; H, 3·9%). The crude anhydride, treated as in the case of the acid chloride, yielded the desired acetoxy-compound (1·3 g.), m. p. 170°.

The *benzoate* formed canary-yellow needles, m. p. 183—184°, from benzene (Found: C, 77·5; H, 3·5. $C_{22}H_{12}O_4$ requires C, 77·6; H, 3·6%). The *methyl ether* formed fine orange needles, m. p. 159—160°, from methanol (Found: C, 76·75; H, 4·1. $C_{16}H_{10}O_3$ requires C, 76·8; H, 4·0%), and its *oxime* canary-yellow needles, m. p. 233—234°, from methanol (Found: N, 5·25. $C_{16}H_{11}O_3N$ requires N, 5·3%).

Ring Closure of cis-γ-Phenyl-γ-(2-furyl)itaconic Acid (I; R = H).—(a) With acetic anhydride and sodium acetate a brown oil was obtained which could not be crystallised.

(b) *With sulphuric acid.* The *cis*-acid (0·54 g.), added slowly to concentrated sulphuric acid (15 c.c.) at 25°, dissolved to a deep green solution. After 15 minutes this was poured into ice-water, and the precipitate collected, washed with water, and recrystallised from acetic acid, giving brick-red needles (0·4 g.), m. p. 192—197°, of *1-keto-3-(2′-furyl)indene-2-acetic acid* (Found: C, 70·4; H, 4·0. $C_{15}H_{10}O_4$ requires C, 70·8; H, 4·0%). The *2 : 4-dinitrophenylhydrazone*, recrystallised from alcohol, had m. p. 215—217° (Found: N, 12·75. $C_{21}H_{14}O_7N_4$ requires N, 12·9%).

The indoneacetic acid (0·8 g.) was boiled for 1½ hours with acetic anhydride (5 c.c.) and anhydrous sodium acetate (0·5 g.). After destruction of the acetic anhydride 0·8 g. of 9-keto-2-acetoxy-3′ : 2′ : 3 : 4-furofluorene, m. p. 170°, was obtained.

Cyclisation of Ethyl Hydrogen trans-*γ-Phenyl-γ-(2-furyl)itaconate: Ethyl 1-Acetoxy-4-(2′-furyl)naphthalene-3-carboxylate* (V; R = Ac, R′ = Et).—The ethyl hydrogen *trans*-ester (61 g.), anhydrous sodium acetate (40 g.), and acetic anhydride (210 c.c.) were boiled for 3 hours, most of the anhydride removed in a vacuum, and the rest poured into water. The dark brown oil solidified. Recrystallised from *iso*propyl ether–ligroin or methanol, the *substance* formed fawn leaflets (55 g.), m. p. 78—81° (Found: C, 70·2; H, 4·9. $C_{19}H_{16}O_5$ requires C, 70·35; H, 5·0%).

Ethyl 1-hydroxy-4-(2′-furyl)naphthalene-3-carboxylate (V; R = H, R′ = Et) was readily formed by warming an alcoholic solution of the 1-acetoxy-derivative with 10% aqueous potassium hydroxide and acidifying the product. Recrystallised from dilute acetic acid, the substance formed fawn needles, m. p. 151—153° (Found: C, 71·9; H, 4·9. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%).

1-Hydroxy-4-(2′-furyl)naphthalene-3-carboxylic Acid (V; R = R′ = H).—The ethyl ester (5 g.), dissolved in spirit (25 c.c.), was boiled with 5% aqueous potassium hydroxide (100 c.c.) for 2 hours. After filtration and neutralisation the *acid* was recrystallised from methanol–hot water (Found: C, 70·6; H, 4·2. $C_{15}H_{10}O_4$ requires C, 70·8; H, 4·0%). It coupled with diazotised aniline, giving a red dye, reduced silver nitrate, and gave with concentrated sulphuric acid a red coloration.

1-Acetoxy-4-(2′-furyl)naphthalene-3-carboxylic acid (V; R = Ac, R′ = H), obtained on acetylating the above acid, recrystallised from acetone–ligroin in fine needles, m. p. 154—156° (Found: C, 68·65; H, 4·2. $C_{17}H_{12}O_6$ requires C, 68·9; H, 4·1%).

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